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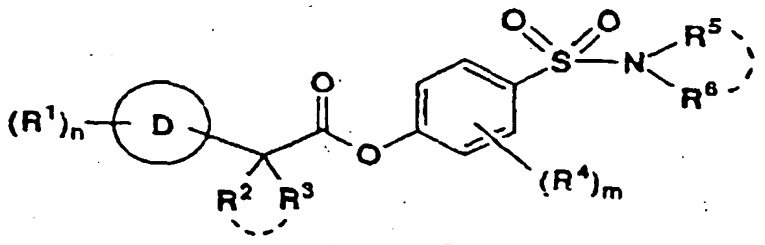
(71) Applicant: **ONO PHARMACEUTICAL CO., LTD.**
Chuo-ku Osaka 541 (JP)

(72) Inventors:
- **Nakae, Takahiko, c/o Minase Research Institute**
  Mishima-gun, Osaka (JP)
- **Kato, Masashi, c/o Minase Research Institute**
  Mishima-gun, Osaka (JP)
- **Fujita, Takehito, c/o Minase Research Institute**
  Mishima-gun, Osaka (JP)
- **Kawabata, Kazuhito,**
  c/o Minase Research Institute
  Mishima-gun, Osaka (JP)
- **Ohno, Hiroyuki, c/o Minase Research Institute**
  Mishima-gun, Osaka (JP)

(74) Representative: **Bentham, Stephen**
J.A. KEMP & CO.
14 South Square
Gray's Inn
London WC1R 5LX (GB)

(54) Sulfonamide derivatives with elastase inhibiting activity

(57) Sulfonamide derivatives of the formula (I)



(I)

wherein R^1 is, *inter alia,* alkyl, alkoxy, hydroxy, keto, nitro, halogen, trihalomethyl, cyano, amidino and -$COOR^7$ (in which R^7 is hydrogen or alkyl),n is an integer from 0 to 5;

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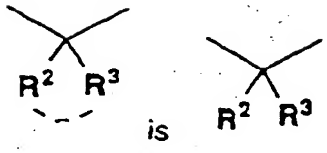
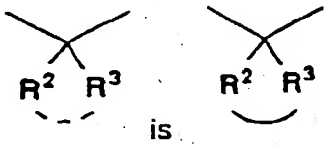
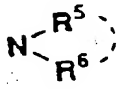
is a carbocyclic ring or heterocyclic ring;



in which R^2 and R^3 each is hydrogen, alkyl, alkoxy, halogen, trihalomethyl or phenyl, or R^2 and R^3, taken together, represent alkylidene, or



in which R^2 and R^3, taken together with the carbon atom to which they are attached represent cycloalkyl;
R^4 is alkyl or alkoxy or two of R^4, attached to the benzene nucleus at ortho positions relative to each other, taken together, represent alkylene; m is an integer from 0 to 4; and



is optionally substituted amino or a nitrogen-containing ring, are described as new pharmaceutical compounds having inhibitory activity or elastase.

Description

This invention relates to sulfonamide derivatives useful as pharmaceuticals. More particularly, this invention relates to:

(1) sulfonamide derivatives of formula (I) as hereinafter defined, and non-toxic salts, acid addition salts and solvates thereof,
(2) processes for their preparation, and
(3) pharmaceutical compositions containing them as active ingredient.

Lysosomal hydrolases of neutrophils have an important role in the defence reaction of organisms against tissue damage caused, for example, by microbes or inflammation.

Elastase and cathepsin G, which are neutral serine proteinases existing locally in azurophil granules, play a part in the decomposition of connective tissue.

In particular, elastase degrades elastic connective tissue by cleaving the cross-linking of elastin which directly maintains the elasticity of e.g. lung tissue, by cleaving the hydrophobic part of protein [J. Cell. Biol., 40, 366 (1969)] and selectively degrading the cross-linking of collagen as well as elastin [J. Biochem., 84, 559 (1978)]. It also acts on tissue proteins such as proteoglycans [J. Clin. Invest., 57, 615 (1976)]. It will be seen therefore that elastase plays an important role in the metabolism of connective tissue.

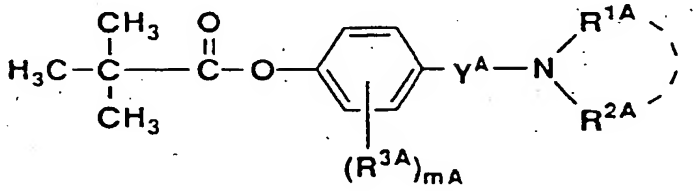
Elastase is inactivated by α_1-proteinase inhibitor (α_1-PI) which is a common inhibitor for serine proteinases in vivo and an imbalance of enzyme and inhibitor causes the destruction of tissue [Schweiz. Med. Wshr., 114, 895 (1984)].

The turnover of elastin in normal tissue is very slow [Endocrinology, 120, 92 (1978)], but pathological acceleration in degradation of elastin is found under various diseased conditions such as pulmonary emphysema [Am. Rev. Respir. Dis., 110, 254 (1974)], atherosclerosis [Lab. Invest., 22, 228 (1970)] and rheumatoid arthritis [in Neutral Proteases of Human Polymorphonuclear Leukocytes, Urban and Schwarzenberg, Baltimore - Munich (1978), page 390], which suggests a relationship between elastase and diseases [Infection Inflammation Immunity, 13, 13 (1983)].

In view of this background, many studies on the development of elastase inhibitors have been conducted recently, and various substances inhibiting elastase have been proposed and many patent applications have been filed.

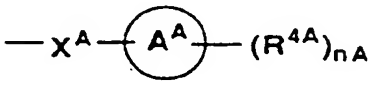
For example,

(1) it is disclosed in EP-A-0347168 that the compound of formula (A)

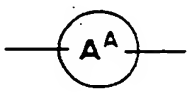


(A)

(wherein Y^A is sulfonyl or carbonyl;
(i) R^{1A} and R^{2A}, which may be the same or different, each represent, inter alia, hydrogen atom, C1-16 alkyl or a group of the formula

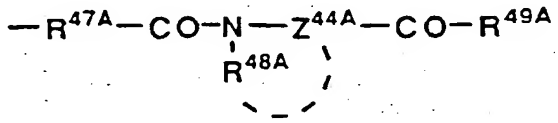


(wherein X^A is bond, sulfonyl, C1-4 alkylene, C1-4 alkyl substituted by -COOH or benzyloxycarbonyl;

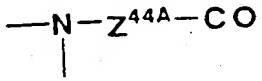


is carbocyclic ring or heterocyclic ring;
nA is 1-5; and

R^{4A} which may be the same or different, represent,
inter alia, hydrogen atom, C1-8 alkyl, C1-14 alkoxy, C1-6 alkylthio, hydroxy, halogen atom, nitro, trihalomethyl, $-Z^{41A}-COOR^{43A}$, $-CONR^{41A}R^{42A}$, a group of the formula

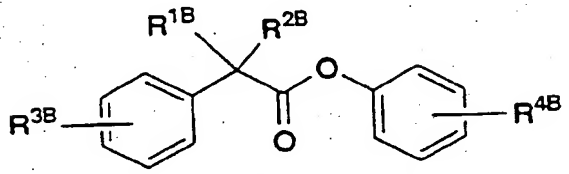


in which the group of formula



is an amino acid residue;
R^{49A} is hydroxy, C1-4 alkoxy, amino, amino or carbamoyl substituted by one or two C1-4 alkyl, etc.) or
(ii) R^{1A} and R^{2A} and the nitrogen atom bonded to R^{1A} and R^{2A} together represent a heterocyclic ring containing at least one nitrogen atom and substituted by -COOH or an unsubstituted heterocyclic ring containing at least one nitrogen atom;
R^{3A} is hydrogen atom, hydroxy, C1-6 alkyl, etc.; and
mA is 1-4)
and non-toxic salts and acid addition salts thereof have an inhibitory activity on elastase ;

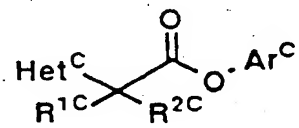
(2) it is disclosed in EP-A-0465802 that the compound of formula (B)



(B)

(wherein R^{1B} and R^{2B}, which may be the same or different, each represent, hydrogen, C1-6 alkyl or C3-6 cycloalkyl, or R^{1B} and R^{2B} taken together represent $-(CH_2)_{nB}-$ (in which nB is 1-6);
R^{3B} is one to five of hydrogen, halogen, C1-12 haloalkyl, C1-12 alkyl, C1-12 alkoxy, C2-12 alkenyl, C3-12 cycloalkyl, mono or bicyclic aryl, $-Z^BR^{5B}$ (in which Z^B is O, S, S(O) or SO_2; R^{5B} is hydrogen, C1-18 alkyl, C3-12 cycloalkyl, or phenyl),$-NR^{6B}R^{7B}$ (in which R^{6B} and R^{7B}, which may be the same or different, each represent hydrogen, C1-12 alkyl, C3-6 cycloalkyl, phenyl, C1-12 alkoxy or $-C(O)-R^{3B}$, or R^{6B} and R^{7B} taken together represent $-C(O)CH_2CH_2-C(O)-$, $-C(O)-C_6H_4-C(O)-$ or $-(CH_2)_{XB}-$ (XB is 2, 3, 4, 5 or 6)), or morpholino, imizazolyl or piperazino, etc., bonded to phenyl ring on nitro atom;and
R^{4B} is one to five of hydrogen, halogen, nitro, $-C(O)CH_3$, $S(O)_{pB}R^{9B}$ (pB is 0, 1 or 2; R^{9B} is hydroxy, -ONa, C1-12 alkyl optionally substituted, cycloalkyl optionally substituted))
and non-toxic pharmaceutically acceptable salts thereof have an inhibitory activity on elastase;

(3) it is disclosed in EP-A-0484949 that the compound of formula (C)



(C)

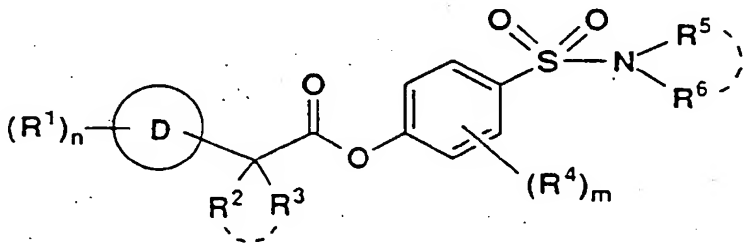
(wherein R^{1C} and R^{2C}, which may be the same or different, each represent hydrogen, C1-6 alkyl or C3-6 cycloalkyl, or R^{1C} and R^{2C} taken together represent $-[CH_2)_{nC}-$ (in which nC is 1-6);

Ar^C is optionally substituted phenyl; and
Het^C is heterocyclic ring containing at least one nitrogen atom, sulfur atom or oxygen atom)
have an inhibitory activity on elastase.

Few of the compounds known to have an inhibitory activity on elastase have been reported to show an inhibitory activity on elastase by oral administration. Most compounds could not be expected to show an effect by oral administration. In order to show activity by oral administration, pharmaceutical agents must be readily absorbed by the digestive organs and must maintain their activity until they are transported to an active site. Therefore, only those compounds having good stability, absorbability and/or solubility in the digestive organs are expected to show sufficient activity by oral administration.

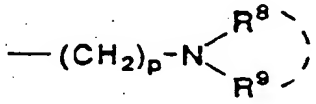
Energetic investigations have been carried out to find new compounds having good inhibitory activity on elastase and also having high safety. As a result, the present inventors have found that these aims may be accomplished by sulfonamide derivatives of the formula (I). Further, we have found that the new compounds have good stability, absorbability and solubility and are active as elastase inhibitors by oral administration.

The present invention provides a sulfonamide derivative of formula (I):

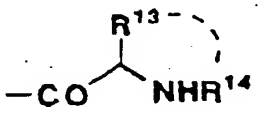


(I)

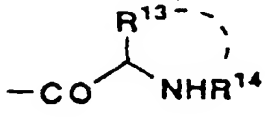
wherein R^1 is C1-8 alkyl, C1-8 alkoxy, hydroxy, keto, nitro, halogen atom, trihalomethyl, cyano, amidino, $-COOR^7$ (in which R^7 is hydrogen atom or C1-8 alkyl), or



(in which p is an integer from 0 to 4, and
R^8 and R^9 each, independently, is hydrogen atom, C1-4 alkyl, C2-5 acyl, $-COOR^{10}$ (in which R^{10} is hydrogen atom or C1-8 alkyl), $-CONR^{11}R^{12}$ (in which R^{11} and R^{12} each, independently, is hydrogen atom or C1-4 alkyl),

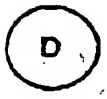


(in which

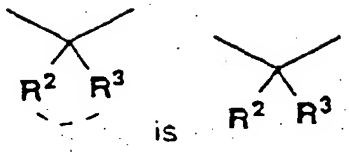


is an α-amino acid residue), or
R^8 and R^9 taken together with the nitrogen atom to which they are attached represent an aliphatic heterocyclic ring which is unsubstituted or substituted by C1-4 alkyl or phenyl C1-4 alkyl);

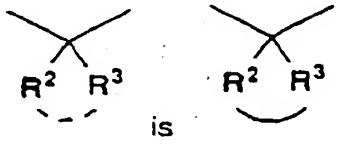
n is an integer from 0 to 5;



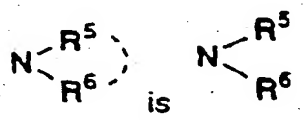
is a carbocyclic ring or heterocyclic ring;



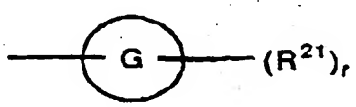
in which R^2 and R^3 each, independently, is hydrogen atom, C1-4 alkyl, C1-4 alkoxy, halogen atom, trihalomethyl or phenyl, or
R^2 and R^3, taken together, represent C1-4 alkylidene, or



in which R^2 and R^3, taken together with the carbon atom to which they are attached represent C3-7 cycloalkyl;
R^4 is C1-4 alkyl or C1-4 alkoxy or two of R^4, attached to the benzene nucleus at ortho positions relative to each other, taken together, represent C3-5 alkylene;
m is an integer from 0 to 4; and

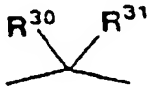


in which R^5 and R^6 each, independently, is
1) hydrogen atom,
2) hydroxy,
3) C1-8 alkyl,
4) C1-8 alkoxy
5) phenyl C1-4 alkoxy,
6) amidino,
7) -M-R^{16}
(in which M is single bond or C1-8 alkylene), and
R^{16} is
i) -$NR^{17}R^{18}$ (in which R^{17} and R^{18} each, independently, is hydrogen atom or C1-4 alkyl),
ii) -$CONR^{19}R^{20}$ (in which R^{19} and R^{20} each, independently, is hydrogen atom or C1-4 alkyl),
iii)

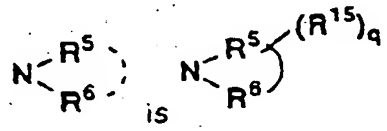


(in which

is a carbocyclic ring,
r is an integer from 0 to 5, and
R^{21} is C1-4 alkyl, C1-4 alkoxy, nitro, amidino, $-COOR^{22}$ (in which R^{22} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl), $-SO_3H$, $-CONR^{23}$-E-R^{24} (in which R^{23} is hydrogen atom or C1-4 alkyl, E is 1-4 alkylene and R^{24} is $-COOR^{25}$ (in which R^{25} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl) or tetrazole ring), tetrazole ring or morpholino ring),
iv) heterocyclic ring, unsubstituted or substituted by 1 to 4 substituents selected from C1-4 alkyl, C1-4 alkoxy, hydroxy, phenyl C1-4 alkyl, $-COOR^{26}$ (in which R^{26} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl), hydroxy C1-4 alkyl or C2-4 alkoxyalkyl),
8) C1-8 alkyl substituted by one or two of $-OR^{27}$ (in which R^{27} is hydrogen atom, C1-4 alkyl, C2-4 alkoxyalkyl or C2-4 alkyl substituted by $-OR^{28}$ (in which R^{28} is hydrogen atom or C2-4 alkoxyalkyl)),
9) -J-$COOR^{29}$ (in which R^{29} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl, and
J is a single bond, $-(CH_2)_s-$ or



(in which s is an integer from 2 to 6, and
R^{30} and R^{31} each, independently, is
i) hydrogen atom,
ii) C1-8 alkyl,
iii) $-COOR^{32}$ (in which R^{32} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl),
iv) carbocyclic or heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, amino, nitro, hydroxy, halogen atom, nitrile, guanidino and amidino, or
v) C1-8 alkyl substituted by one or more substituents selected from hydroxy, $-COOR^{33}$ (in which R^{33} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl), $-NR^{34}R^{35}$ (in which R^{34} and R^{35} each, independently, is hydrogen atom or C1-4 alkyl), carbocyclic or heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, amino, nitro, hydroxy, halogen atom, nitrile, guanidino and amidino, with the proviso that a carbon atom of C1-8 alkyl may be replaced by a sulfur atom), or



in which R^5 and R^6, taken together with the nitrogen atom to which they are attached represent a heterocyclic ring,
q is an integer from 0 to 4, and
R^{15} is
1) hydroxy,
2) keto,
3) protected keto,
4) C1-4 alkyl,
5) C1-4 alkoxy,
6) phenyl,
7) phenoxy,
8) phenyl C1-4 alkyl,

9) phenyl C1-4 alkoxy,
10) nitro,
11)-$COOR^{36}$ (in which R^{36} is hydrogen atom, C1-8 alkyl, C1-4 alkyl substituted by -$CONR^{37}R^{38}$ (in which R^{37} and R^{38} each, independently, is hydrogen atom or C1-4 alkyl), C1-4 alkyl substituted by -$NR^{39}R^{40}$ (in which R^{39} and R^{40} each, independently, is hydrogen atom or C1-4 alkyl), C1-4 alkyl substituted by -OR^{41} (in which R^{41} is C2-4 alkyl substituted by -OR^{42} (in which R^{42} is hydrogen atom or C2-4 alkoxyalkyl)) or C1-4 alkyl substituted by piperazino ring),
12) -$NR^{43}R^{44}$ (in which R^{43} and R^{44} each, independently, is hydrogen atom, C1-4 alkyl or C2-5 acyl),
13) -$CONR^{45}R^{46}$ (in which R^{45} and R^{46} each, independently, is hydrogen atom, hydroxy, C1-4 alkyl, phenyl C1-4 alkyloxy or C1-4 alkyl substituted by hydroxy or -$COOR^{47}$ (in which R^{47} is hydrogen atom or C1-8 alkyl),),
14) C1-4 alkyl substituted by one or more substituents selected from hydroxy, -$COOR^{48}$ (in which R^{48} is hydrogen atom or C1-8 alkyl), -$NR^{49}R^{50}$ (in which R^{48} and R^{50} each, independently, is hydrogen atom or C1-4 alkyl), -OSO_3H or 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,
15) 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,
16) halogen atom,
17) -CHO, or
18) -NR^{51}-$COOR^{52}$ (in which R^{51} and R^{52} each, independently, is hydrogen atom or C1-8 alkyl);
or a non-toxic salt, acid addition salt or solvate thereof.

The sulfonamide derivatives of the present invention are novel compared with compounds disclosed in the prior art.

To summarize, the compounds of formula (A) described in EP-A-0347168 necessarily contain a pivaloyloxy group. In contrast, the compounds of the present invention have a ring D which may be substituted by various substituents R^1.

Thus the compounds of the present invention have a chemical structure quite different from that of the compounds of formula (A).

The compounds of formula (B) described in EP-A-0465802 include compounds in which R^{4B} represents $S(O)_{pB}R^{9B}$. R^{9B} can represent hydroxy, -ONa, optionally substituted C1-12 alkyl cr optionally substituted cycloalkyl, but can not represent amino group. Further, the compounds of formula (C) described in EP-A-0484949 include those in which a substituent of Ar^C represents $S(O)_{pC}R^{9C}$. R^{9C} can represent hydroxy, -ONa, optionally substituted C1-12 alkyl or optionally substituted cycloalyl, but can not represent amino group.

In contrast, the compounds of the present invention have a sulfonamide group which may be substituted by various substituents. Thus the compounds of the present invention have a chemical structure quite different from that of the compounds of formula (B) and (C).

Furthermore, related compounds show no activity by oral administration, but some compounds in the present invention have good stability, absorbability and solubility, and are, therefore, active as elastase inhibitors by oral administration.

In the formula (I), C1-4 alkyl represented by R^2, R^3, R^4, R^8, R^9, R^{11}, R^{12}, R^{15}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{23}, R^{27}, R^{34}, R^{35}, R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{43}, R^{44}, R^{45}, R^{46}, R^{49}, R^{50}, and substituents of aliphatic heterocyclic ring, carbocyclic ring or heterocyclic ring means methyl, ethyl, propyl, butyl and isomers thereof.

In the formula (I), C1-8 alkyl represented by R^1, R^5, R^6, R^7, R^{10}, R^{22}, R^{25}, R^{26}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{36}, R^{47}, R^{48}, R^{51} and R^{52} means methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl and isomers thereof.

In the formula (I), C2-4 alkyl represented by R^{27} and R^{41} means ethyl, propyl, butyl and isomers thereof.

In the formula (I), C3-5 alkylene represented by two of R^4 attached at ortho positions relative to each other means trimethylene, tetramethylene, pentamethylene, and isomers thereof.

In the formula (I), C1-8 alkylene represented by M means methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, heptamethylene, octamethylene and isomers thereof.

In the formula (I), C1-4 alkylene represented by E means methylene, ethylene, trimethylene, tetramethylene and isomers thereof.

In the formula (I), phenyl C1-4 alkyl or phenyl C1-4 alkoxy means C1-4 alkyl or C1-4 alkoxy substituted by a phenyl group.

In the formula (I), phenyl C1-4 alkyl represented by R^{29}, R^{32}, R^{33}, R^{15} and substituents of aliphatic heterocyclic ring or heterocyclic ring means methyl, ethyl, propyl, butyl and isomers thereof, which are substituted by a phenyl group.

In the formula (I), phenyl C1-4 alkoxy represented by R^5, R^6, R^{15}, R^{45} and R^{46} means methoxy, ethoxy, propoxy, butoxy and isomers thereof, which are substituted by a phenyl group.

In the formula (I), C2-5 acyl represented by R^8, R^9, R^{43} and R^{44} means acetyl, propionyl, butyryl, valeryl and isomers thereof.

In the formula (I), C2-4 alkoxyalkyl represented by R^{27}, R^{28}, R^{42} and substituent of heterocyclic ring means methoxymethyl, ethoxymethyl, propoxymethyl, methoxyethyl, ethoxyethyl, methoxypropyl and isomers thereof.

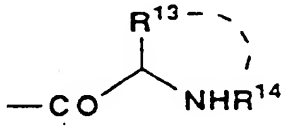
In the formula (I), C1-8 alkoxy represented by R^1, R^5 and R^6 means methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy, heptyloxy, octyloxy and isomers thereof.

In the formula (I), C1-4 alkoxy represented by R^2, R^3, R^4, R^{15}, R^{21} and substituents of carbocyclic ring or hetero-

cyclic ring means methoxy, ethoxy, propoxy, butoxy and isomers thereof.

In the formula (I), halogen atom represented by R^1, R^2, R^3 and R^{15} means fluorine, chlorine, bromine and iodine.

In the formula (I), the α-amino acid residue represented by



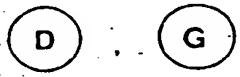
may be any α-amino acid residue. For example, it may be a residue of glycine, alanine, serine, threonine, cystine, valine, methionine, leucine, isoleucine, phenylalanine, tyrosine, tryptophan, aspartic acid, glutamic acid, arginine, glutamine, lysine, histidine or proline.

In the formula (I), C3-7 cycloalkyl represented by R^2 and R^3, taken together with the carbon atom to which they are attached means cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

In the formula (I), C1-4 alkylidene represented by R^2 and R^3, taken together, means methylidene, ethylidene, propylidene, butylidene and isomers thereof.

In the formula (I), aliphatic heterocyclic ring represented by R^8 and R^9, taken together with the nitrogen atom to which they are attached preferably means 5-15 membered mono- or bi-cyclic saturated heterocyclic ring or partly saturated heterocyclic ring containing one or two nitrogen atoms or one nitrogen atom and one sulfur atom or oxygen atom. Examples include pyrroline, pyrrolidine, imidazoline, imidazolidine, pyrazoline, pyrazolidine, piperidine, piperazine, tetrahydropyrimidine, hexahydropyrimidine, tetrahydropyridazine, hexahydropyridazine, hexahydroazepine, dihydrooxazole, tetrahydrooxazole, dihydroisooxazole, tetrahydroisooxazole, dihydrothiazole, tetrahydrothiazole, dihydroisothiazole, tetrahydroisothiazole, morpholine, thiomorpholine, indoline, isoindoline, dihydroindazole, perhydroindazole, dihydroquinoline, tetrahydroquinoline, perhydroquinoline, dihydroisoquinoline, tetrahydroisoquinoline, perhydroisoquinoline, dihydrophthalazine tetrahydrophthalazine, perhydrophthalazine, dihydronaphthyridine, tetrahydronaphthyridine, perhydronaphthyridine, dihydroquinoxaline, tetrahydroquinoxaline, perhydroquinoxaline, dihydroquinazoline, tetrahydroquinazoline, perhydroquinazoline, dihydrocinnoline, tetrahydrocinnoline, perhydrocinnoline, dihydrobenzoxazole, perhydrobenzoxazole, dihydrobenzothiazole, perhydrobenzothiazole, dihydrobenzoimidazole and perhydrobenzoimidazole rings.

In the formula (I), carbocyclic ring represented by



$R^{30}$and R^{31} preferably means 3-15 membered mono- or poly-cyclic aromatic hydrocarbon ring or aliphatic hydrocarbon ring. Examples include cyclopentadiene, benzene, pentalene, indene, naphthalene, azulene, cyclopropane, cyclobutane, cyclopentane, cyclopentene, cyclohexane, cyclohexene, cyclohexadiene, cycloheptane, dihydroindene, perhydroindene, dihydronaphthalene, tetrahydronaphthalene, perhydronaphthalene, bicyclo[2.2.1]heptane, bicyclo[3.2.2] nonane and adamantane rings.

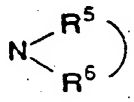
When the above. carbocyclic ring has two equivalents, bond sites exist on the same carbon atom or different carbon atom, ie. when the ring contains two free valencies, two substituents may be attached to the same carbon atom or to different carbon atoms.

In the formula (I), heterocyclic ring represented by

R^{16}, R^{30} and R^{31} preferably means 5-15 membered mono- or bi-cyclic aromatic heterocyclic ring, saturated heterocyclic ring or partly saturated heterocyclic ring containing one to four nitrogen atoms, one or two sulfur atoms, one or two oxygen atoms or one nitrogen atom and one sulfur atom or oxygen atom. Examples include pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, azepine, diazepine, furan, pyran, oxepine, thiophene, thiaine (thiopyran), thiepine, oxazole, isooxazole, thiazole, isothiazole, oxazine, oxazepine, thiazine, thiazepine, indole, isoindole, benzo-

furan, isobenzofuran, benzothiophene, isobenzothiophene, indazole, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, benzoxazole, benzothiazole, benzoimidazole, pyrroline, pyrrolidine, imidazoline, imidazolidine, pyrazoline, pyrazolidine, piperidine, piperazine, tetrahydropyrimidine, hexahydropyrimidine, tetrahydropyridazine, hexahydropyridazine, hexahydroazepine, hexahydrodiazepine, dihydrofuran, tetrahydrofuran, dihydropyran, tetrahydropyran, dihydrothiophene, tetrahydrothiophene, dihydrothiaine (dihydrothiopyran), tetrahydrothiaine (tetrahydrothiopyran), dihydrooxazole, tetrahydrooxazole, dihydroisooxazole, tetrahydroisooxazole, dihydrothiazole, tetrahydrothiazole, dihydroisothiazole, tetrahydroisothiazole, morpholine, thiomorpholine, indoline, isoindoline, dihydrobenzofuran, perhydrobenzofuran, dihydroisobenzofuran, perhydroisobenzofuran, dihydrobenzothinphene, perhydrobenzothiophene, dihydroisobenzothiophene, perhydroisobenzothiophene, dihydroindazole, perhydroindazole, dihydroquinoline, tetrahydroquinoline, perhydroquinoline, dihydroisoquinoline, tetrahydroisoquinoline, perhydroisoquinoline, dihydrophthalazine, tetrahydrophthalazine, perhydrophthalazine, dihydronaphthyridine, tetrahydronaphthyridine perhydronaphthyridine, dihydroquinoxaline, tetrahydroquinoxaline, perhydroquinoxaline, dihydroquinazoline, tetrahydroquinazoline, perhydroquinazoline, dihydrocinnoline, tetrahydrocinnoline, perhydrocinnoline, dihydrobenzoxazole perhydrobenzoxazole, dihydrobenzothiazole, perhydrobenzothiazole, dihydrobenzoimidazole, perhydrobenzoimidazole, dihydrobenzoxazine, 1,3-dioxaindan, 1,4-benzodioxane, quinuclidine, triazole and tetrazole rings.

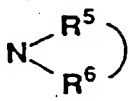
In the formula (I), heterocyclic ring represented by



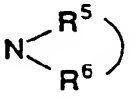
that is, R^5 and R^6, taken together with the nitrogen atom to which they are attached, preferably means 3-15 membered mono- or bi-cyclic aromatic heterocyclic ring, saturated heterocyclic ring or partly saturated heterocyclic ring containing one or two nitrogen atoms or one nitrogen atom and one sulfur atom or oxygen atom. Examples include pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, azepine, diazepine, aziridine, azetidine, pyrroline, pyrrolidine, imidazoline, imidazolidine, pyrazoline, pyrazolidine, piperidine, piperazine, tetrahydropyrimidine, hexahydropyrimidine tetrahydropyridazine, hexahydropyridazine, hexahydroazepine, hexahydrodiazepine, oxazole, isooxazole, thiazole, isothiazole, oxazine, oxazepine, thiazine, thiazepine, indole, isoindole, indazole, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, benzoxazole, benzothiazole, benzoimidazole, dihydrooxazole, tetrahydrooxazole, dihydroisooxazole, tetrahydroisooxazole, dihydrothiazole, tetrahydrothiazole, dihydroisothiazole, tetrahydroisothiazole, morpholine, thiomorpholine, indoline, isoindoline, perhydroindole, dihydroindazole, perhydroindazole, dihydroquinoline, tetrahydroquinoline, perhydroquinoline, dihydroisoquinoline, tetrahydroisoquinoline, perhydroisoquinoline, dihydrophthalazine, tetrahydrophthalazine, perhydrophthalazine, dihydronaphthyridine, tetrahydronaphthyridine, perhydronaphthyridine, dihydroquinoxaline, tetrahydroquinoxaline, perhydroquinoxaline, dihydroquinazoline, tetrahydroquinazoline, perhydroquinazoline, dihydrocinnoline, tetrahydrocinnoline, perhydrocinnoline, dihydrobenzoxazole, perhydrobenzoxazole, dihydrobenzothiazole, perhydrobenzothiazole, dihydrobenzoimidazole, perhydrobenzoimidazole, 7-azabicyclo[3.2.1]octane, and 3-azabicyclo[3.2.2]nonane rings.

In the formula (I), 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms represented by R^{15} means, for example, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, pyrroline, pyrrolidine, imidazoline, imidazolidine, pyrazoline, pyrazolidine, piperidine, piperazine, tetrahydropyrimidine or tetrahydropyridazine.

In the formula (I), examples of the ring represented by



to which a protected keto group is bonded, include 1,3-dioxolane and spiro ring derivatives of



One or two keto groups (=O) may be attached to the same or different sulfur atoms as substituents R^{15}. One group is treated as one R^{15}.

In formula (I):-

m preferably represents 0, 1 or 2, more preferably 0 or 1.

R^4 preferably represents alkyl or alkoxy of 1-4 carbon atoms, for example methyl, ethyl, isopropyl, methoxy, ethoxy or isopropoxy. Methyl is especially preferred. When one or two substituents R^4 are present they preferably occupy one or both positions adjacent to the oxygen atom attached to the phenyl ring; compounds in which two substitutents are present on the positions ortho and meta to the oxygen attached to the phenyl ring also constitute a feature of the invention; two such substituents may together form a five membered ring fused to the phenyl ring.

Compound in which m is 1 and R^4 represents methyl in the ortho position relative to the oxygen atom attached to the phenyl ring are especially preferred.

One of R^2 and R^3 preferably represents hydrogen, methyl, ethyl, or methoxy and the other represents methyl, ethyl, isopropyl, phenyl or trifluoromethyl or R^2 and R^3 together with the carbon atom to they are attached represent ethylidene or cycloalkyl of 3-6 carbon atoms. The ethyl group represented by one of R^2 and R^3 is preferably in β-configuration.

D preferably represents phenyl, naphthyl (preferably 1-or 2-naphthyl), thiophenyl (preferably thiophen-2-yl), cyclohexyl, pyridinyl, (preferably pyridin-3-yl), thiazolyl (preferably thiazol-4-yl) imidazolinyl (preferably imidazolin-2-yl), benzimidazolyl (preferably benzimidazol 5-yl), 2H-1,4-benzoxazin-3-on-6-yl, or 1,3-benzodioxol-5-yl, or 1H-1-methyl-2-pyridon-3-yl. Phenyl is especially preferred.

n preferably represents 0,1,2 or 3, preferably 0 or 1. R^1 preferably represents alkyl of 1-4 carbon atoms e.g. methyl; alkoxy of 1-4 carbon atoms, e.g. methoxy; amino; amino substituted by two alkyl groups each of 1-4 carbon atoms, for example dimethylamino; methyl substituted by carbamoyl; methyl substituted by alkanoyl of 2-5 carbon atoms for example by acetyl; nitro; hydroxy; cyano; carboxy, trihalomethyl, e.g. trifluoromethyl; amidino; amino substituted by alkoxycarbonyl; halogen, e.g. chlorine; pyrrolidinyl; piperidinyl; perhydroazepinyl; or morpholinyl or piperazinyl optionally substituted on the 4-position by benzyl.

Compounds in which D represents mono substituted phenyl constitute a feature of the invention: when D is substituted phenyl at least one substituent is preferably on the 4-position. Preferred 4-substituted phenyl groups are those in which the substituent is a 5-, 6- or 7-membered nitrogen-containing ring attached to phenyl via the nitrogen atom: pyrrolidin-1-yl is preferred.

In the grouping NR^5R^6, when R^5 and R^6, taken together with the nitrogen atom to which they are attched do not represent a heterocyclic ring, the grouping NR^5R^6 preferably represents hydrogen; methyl; ethyl; propyl; methoxy; benzyl; methoxymethoxyethyl; 1-hydroxyethyl; hydrogen is especially preferred, and the other represents phenyl; phenyl substituted substituents, e.g. 2-((1-carboxymethyl)aminocarbonyl)phenyl, 4-nitrophenyl; heterocyclic ring, e.g. quinuclidine, piperidine, pyridine, imidazole, morpholine, tetrazole; C1-8 alkyl substituted by heterocyclic ring, e.g. piperazin-1-ylethyl, piperadin-1-ylethyl, morpholin-1-ylethyl, pyridin-2-ylethyl, pyrrol-2-ylethyl; morpholin-1-ylethyl is especially preferred.

In the grouping NR^5R^6, when R^5 and R^6, taken together with the nitrogen atom to which they are attched represent a heterocyclic ring, the ring preferably represents pyrrolidine; indole; indoline; perhydroindole; benzoimidazole; morpholine; piperidine; piperazine; 7-azabicyclo[3.2.1]octane, 3-azabicyclo[3.2.2]nonane; tetrahydrooxazole; tetrahydrothiazole; imidazole; hexahydrodiazepine; aziridine; azetidine; piperazine is especially preferred.

In the grouping NR^5R^6, when R^5 and R^6, taken together with the nitrogen atom to which they are attched represent a heterocyclic ring, R^{15} preferably represents hydroxy; C1-4 alkyl substituted by a hydroxy, e.g. hydroxymethyl; C1-4 alkyl substituted by a heterocyclic ring, e.g. pyrrolidin-1-ylmethyl; benzyloxy; amino; methoxy; dimethylamino; acetylamino; methy., nitro; halogen, e.g. fluorine; keto; carboxy; ester, e.g. ethoxycarbonyl, t-butoxycarbonyl, 2-aminoethoxycarbonyl, 2-(2-hydroxyethoxy)ethoxycarbonyl, 2-(piperazin-1-yl)ethoxycarbonyl; amide, e.g. carboxymethylaminocarbonyl; carboxy is especially preferred.

In the grouping NR^5R^6, when R^5 and R^6, taken together with the nitrogen atom to which they are attched represent a heterocyclic ring, q preferably represents 0, 1 or 2, more preferably 0 or 1.

Throughout the specification including claims, it may be easily understood by those skilled in the art, that all isomers are included in the present invention. For example, the alkyl, alkylene and alkenylene groups include straight-chain and also branched-chain ones. Double bond in alkenylene includes E, Z and EZ mixture. Accordingly, all isomers produced by the existence of asymmetric carbon atoms are included in the present invention when groups such as branched-chain alkyl are present.

The compounds of the formula (I), of the present invention may be converted into the corresponding non-toxic salts or acid addition salts by methods known *per se*.

Water-soluble salts are preferred. Suitable salts, for example, include salts of alkali metals (e.g. potassium or sodium), salts of alkaline earth metals (e.g. calcium or magnesium), ammonium salts, salts of pharmaceutically-acceptable organic amines (e.g. tetramethylammonium, triethylamine, methylamine, dimethylamine, cyclopentylamine,

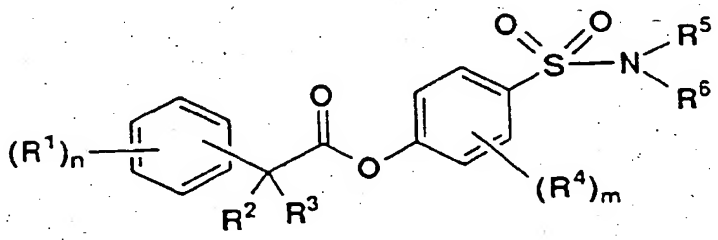
benzylamine, phenethylamine, piperidine, monoethanolamine, diethanolamine, tris(hydroxymethyl)amine, lysine, arginine or N-methyl-D-glucamine).

Water-soluble acid addition salts are also preferred. Suitable acid addition salts, for example, include the salts with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid and nitric acid, and the salts with organic acids such as acetic acid, trifluoroacetic acid, lactic acid, tartaric acid, oxalic acid, fumaric acid, maleic acid, benzenesulfonic acid, toluenesulfonic acid, isethionic acid, glucuronic acid and gluconic acid.

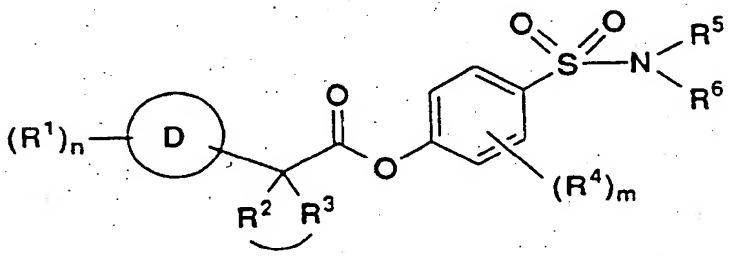
The compounds of the formula (I) or salts, of the present invention may be converted into the corresponding solvates by methods known *per se*.

Water-soluble solvates are preferred. Suitable solvates, for example, include the salts with water or with alcohol solvents such as ethanol.

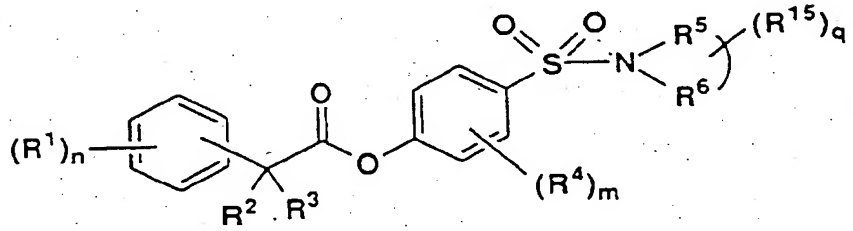
Preferred compounds of the present invention are of the following formulae (I-A1), (I-A2), (I-B1) and (I-B2).



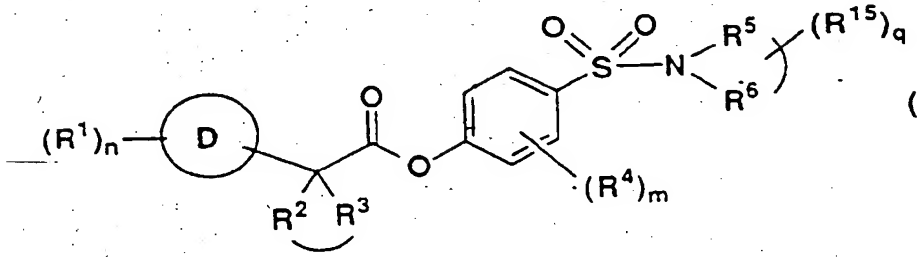
(I-A1)



(I-A2)



(I-B1)



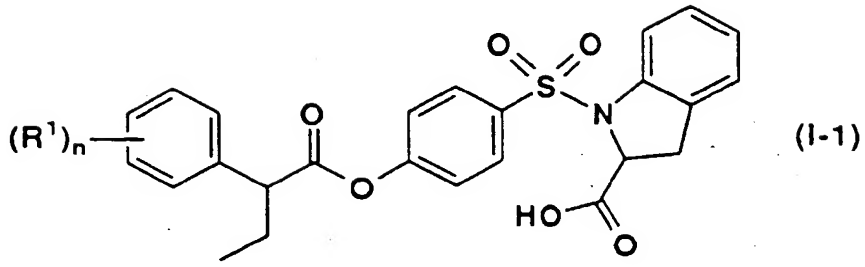
(I-B2)

(wherein all symbols are as hereinbefore defined).

Representative compounds of the present invention are illustrated by the compounds in the following Tables 1-46 and the non-toxic salts and acid addition salts thereof.

In the Tables, Me is methyl, Et is ethyl, Pr is propyl, iPr is isopropyl and tBu is tert-butyl.

Table 1



(I-1)

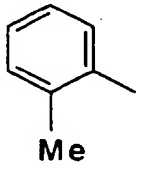
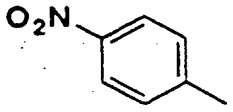
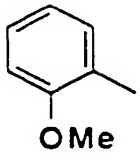
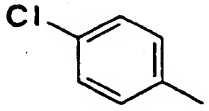
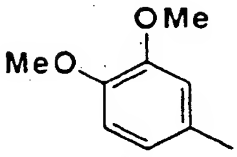
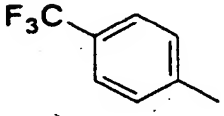
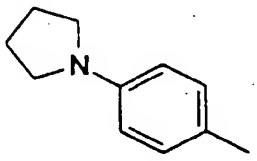
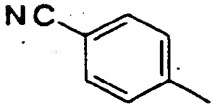
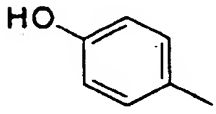
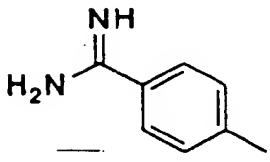
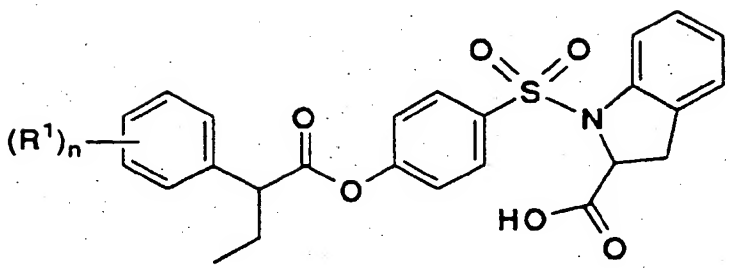
No.	$(R^1)_n$	No.	$(R^1)_n$
1		6	
2		7	
3		8	
4		9	
5		10	

Table 1(continued)



(I-1)

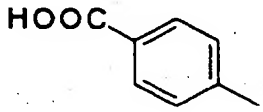
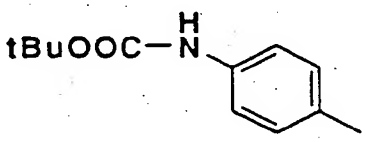
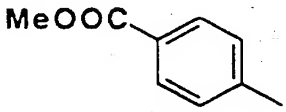
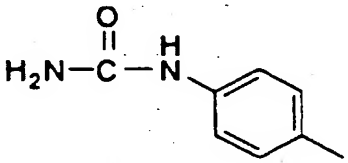
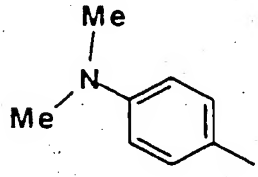
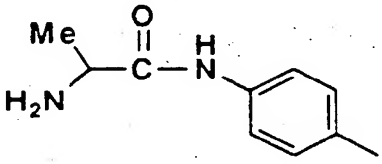
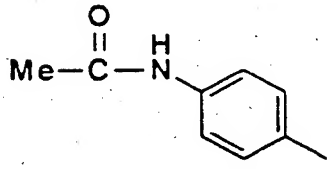
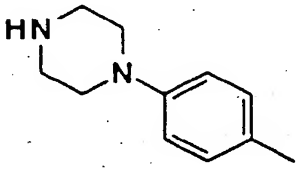
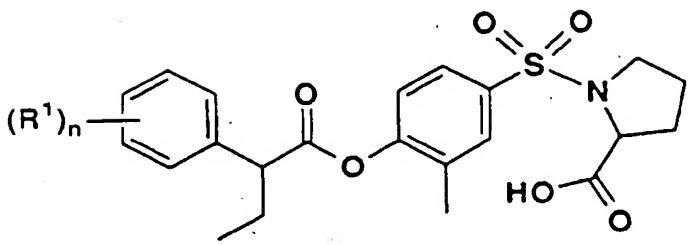
No.	$(R^1)_n$	No.	$(R^1)_n$
11		15	
12		16	
13		17	
14		18	

Table 2



(I-2)

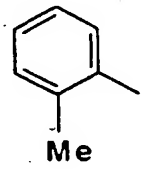
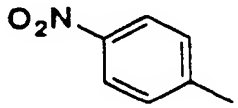
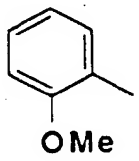
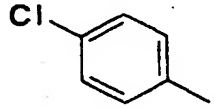
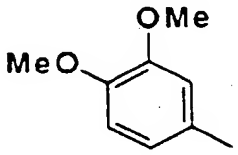
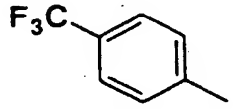
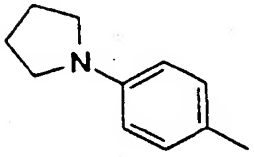
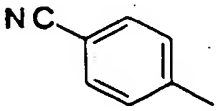
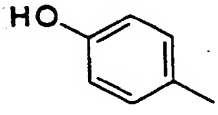
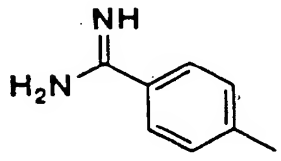
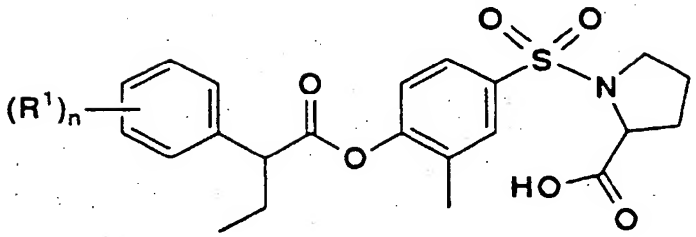
No.	$(R^1)_n$	No.	$(R^1)_n$
1		6	
2		7	
3		8	
4		9	
5		10	

Table 2 (continued)



(I-2)

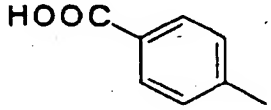
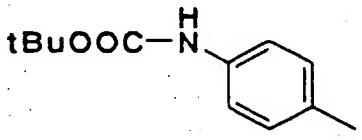
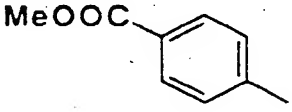
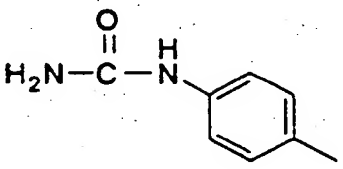
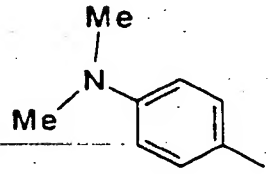
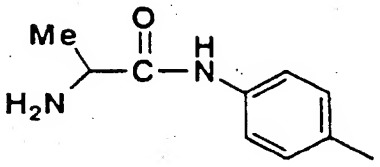
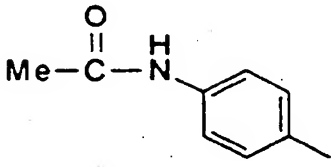
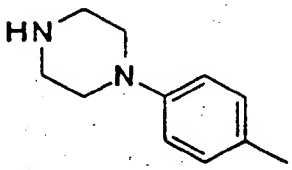
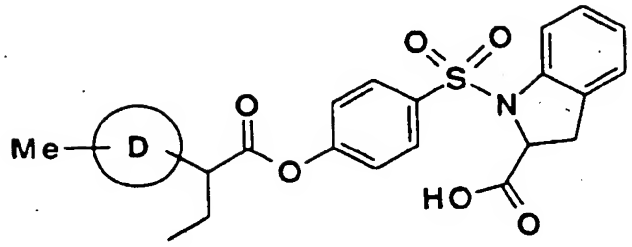
No.	$(R^1)_n$	No.	$(R^1)_n$
11		15	
12		16	
13		17	
14		18	

Table 3



(I-3)

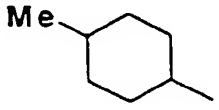
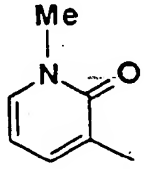
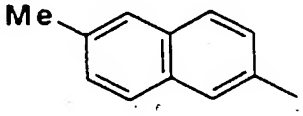
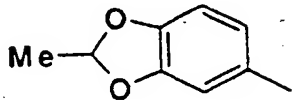
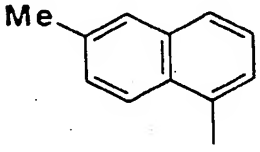
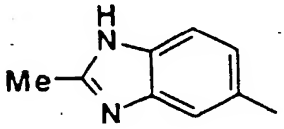
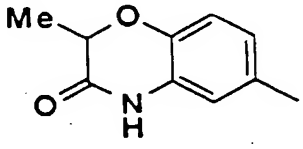
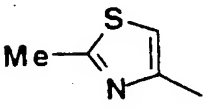
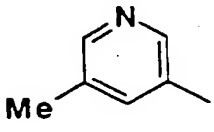
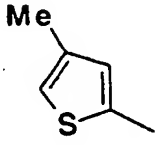
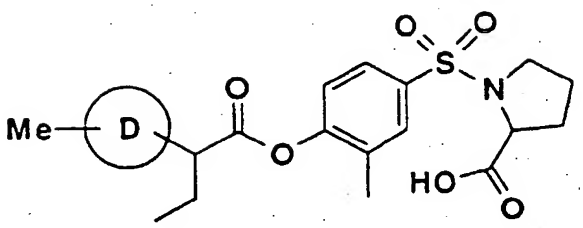
No.	Me–D–	No.	Me–D–
1		6	
2		7	
3		8	
4		9	
5		10	

Table 4



(I-4)

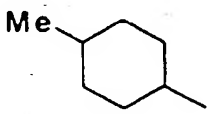
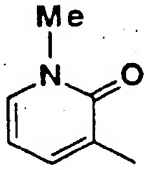
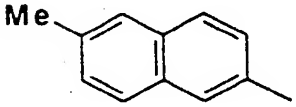
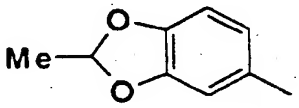
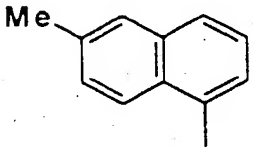
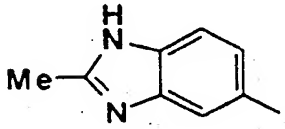
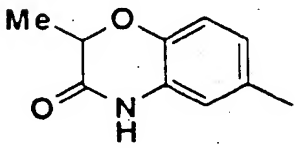
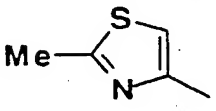
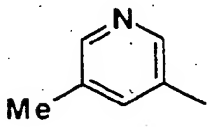
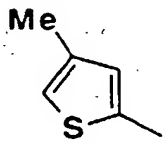
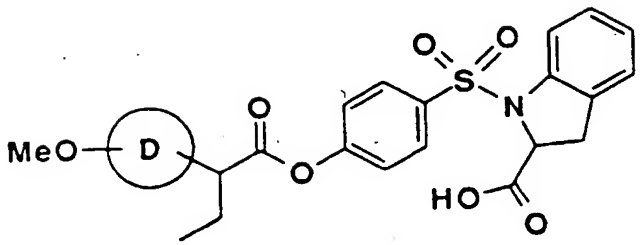
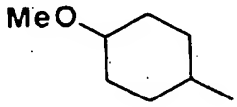
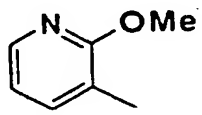
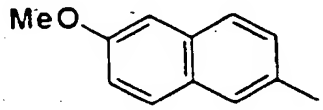
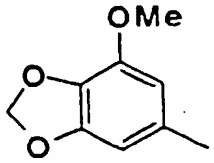
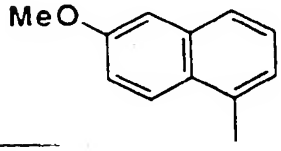
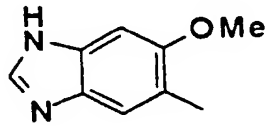
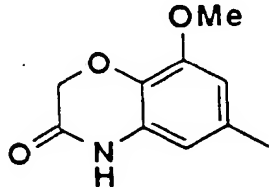
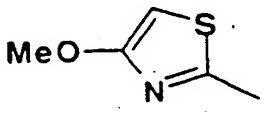
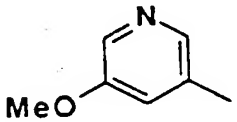
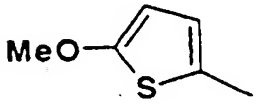
No.	Me–D	No.	Me–D
1		6	
2		7	
3		8	
4		9	
5		10	

Table 5



(I-5)

No.	MeO-D-	No.	MeO-D-
1		6	
2		7	
3		8	
4		9	
5		10	

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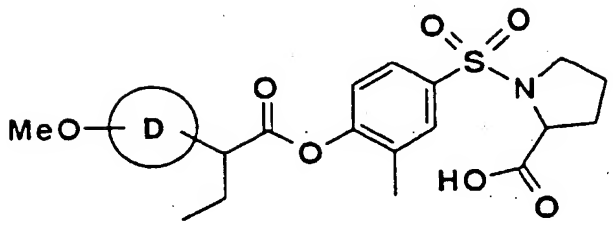
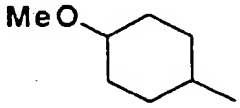
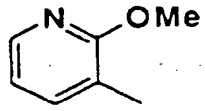
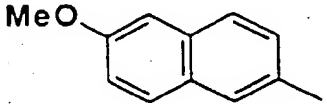
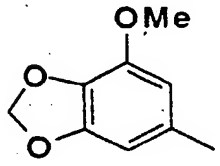
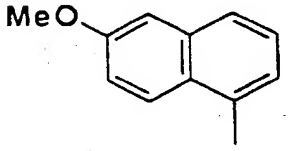
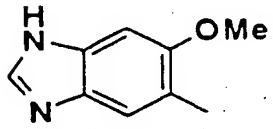
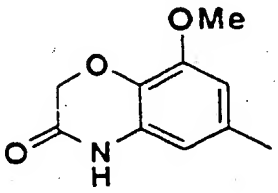
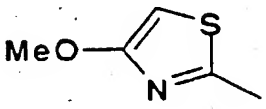
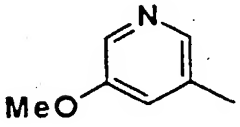
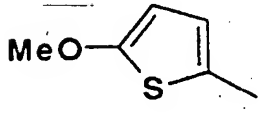


(I-6)

No.	MeO–D–	No.	MeO–D–
1		6	
2		7	
3		8	
4		9	
5		10	

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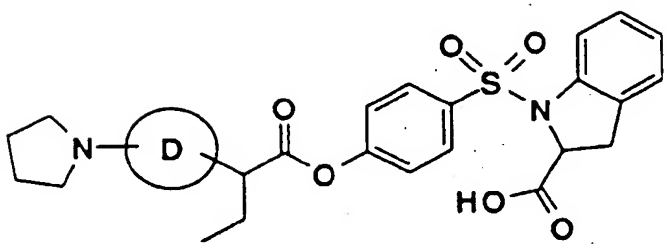
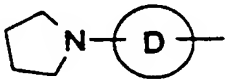
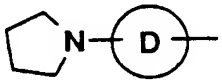
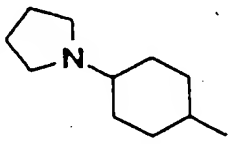
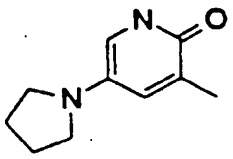
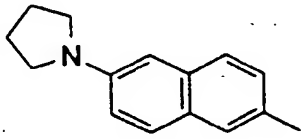
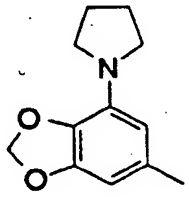
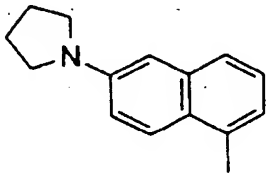
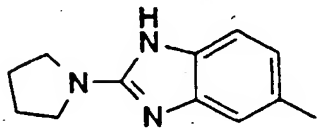
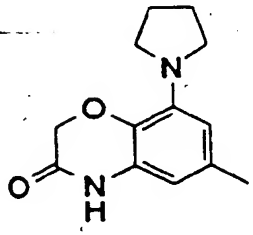
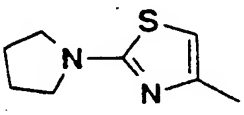
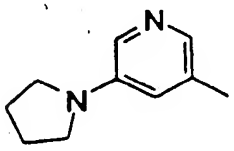
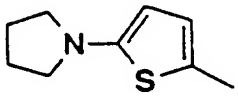


(I-7)

No.		No.	
1		6	
2		7	
3		8	
4		9	
5		10	

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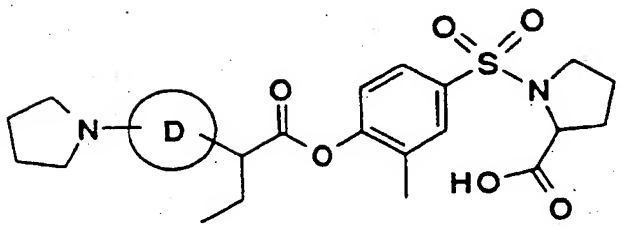
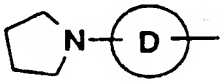
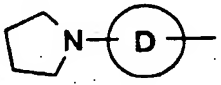
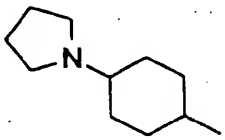
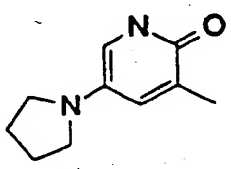
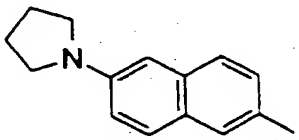
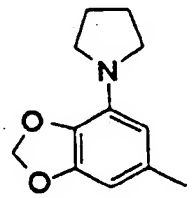
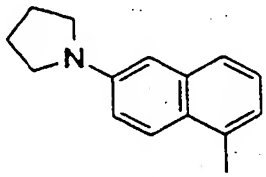
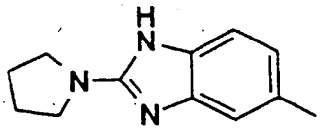
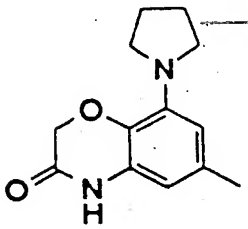
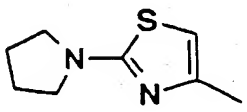
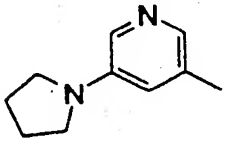
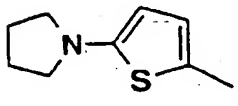


(I-8)

No.		No.	
1		6	
2		7	
3		8	
4		9	
5		10	

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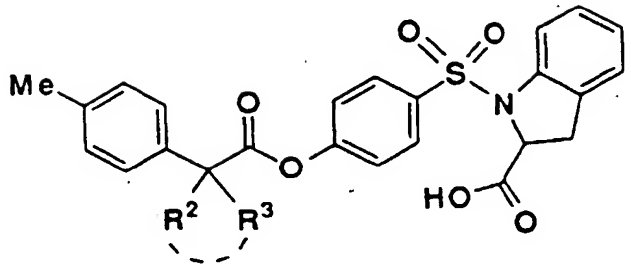
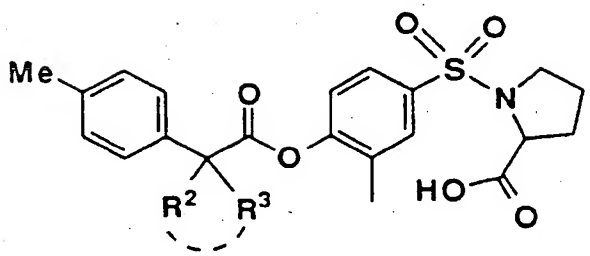


(I-9)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

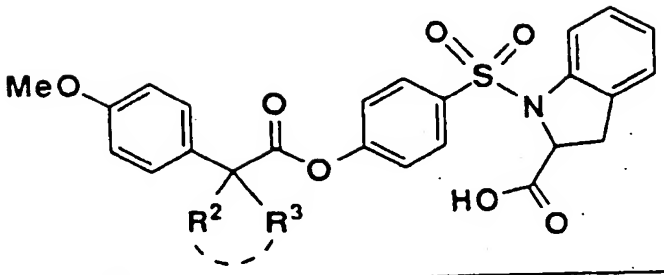
Table 10



(I-10)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

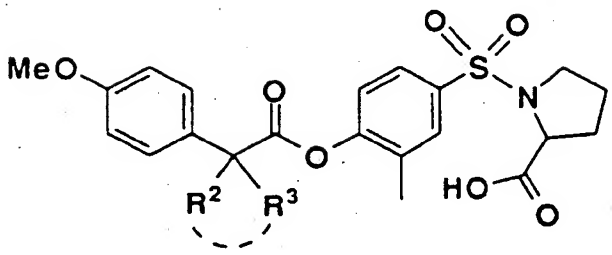
Table 11



(I-11)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

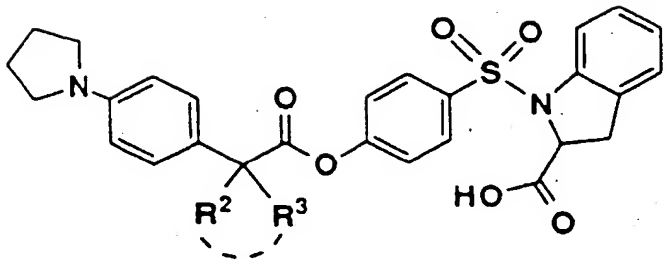
Table 12



(I-12)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

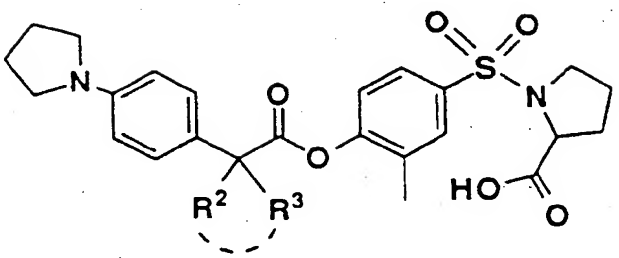
Table 13



(I-13)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

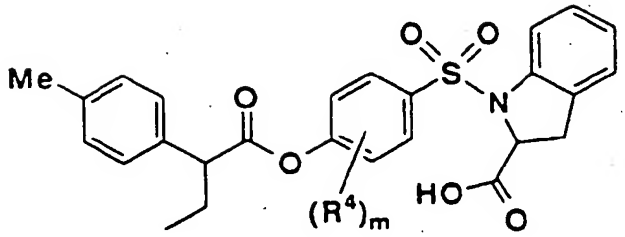
Table 14



(I-14)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

Table 15



(I-15)

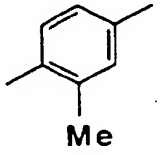
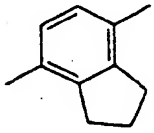
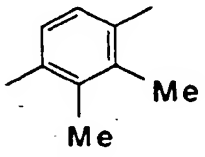
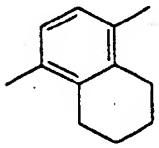
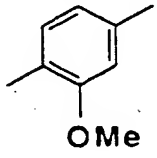
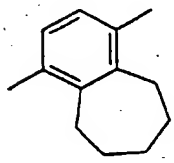
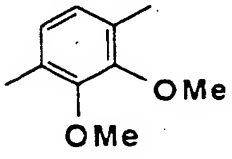
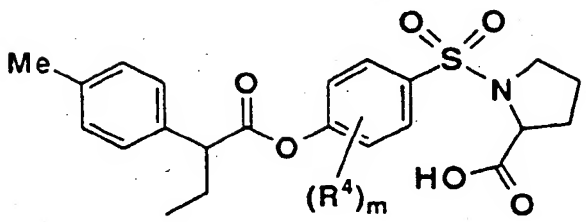
No.	$(R^4)_m$	No.	$(R^4)_m$
1		5	
2		6	
3		7	
4			

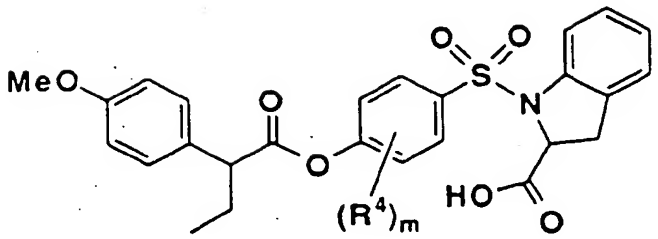
Table 16



(I-16)

No.	$(R^4)_m$	No.	$(R^4)_m$
1	Me	5	
2	Me, Me	6	
3	OMe	7	
4	OMe, OMe		

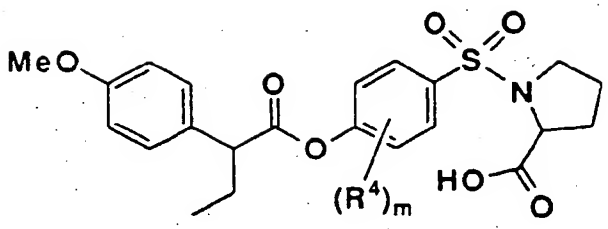
Table 17



(I-17)

No.	$(R^4)_m$	No.	$(R^4)_m$
1	Me	5	
2	Me, Me	6	
3	OMe	7	
4	OMe, OMe		

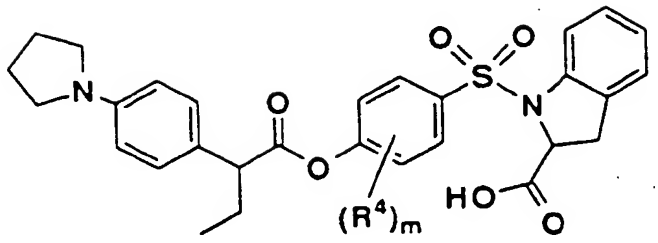
Table 18



(I-16)

No.	$(R^4)_m$	No.	$(R^4)_m$
1	Me	5	
2	Me, Me	6	
3	OMe	7	
4	OMe, OMe		

Table 19



(I-19)

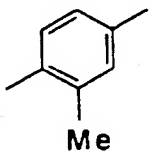
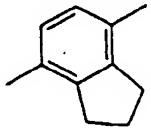
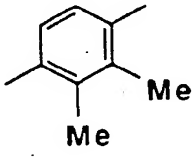
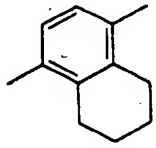
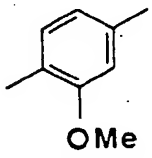
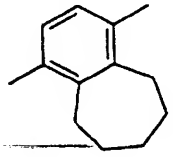
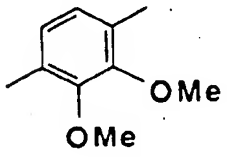
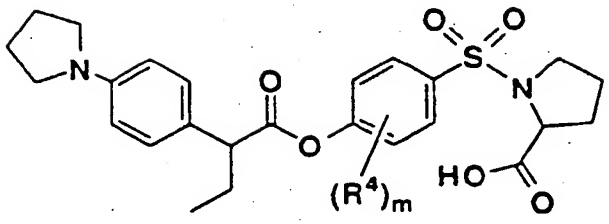
No.	$(R^4)_m$	No.	$(R^4)_m$
1		5	
2		6	
3		7	
4			

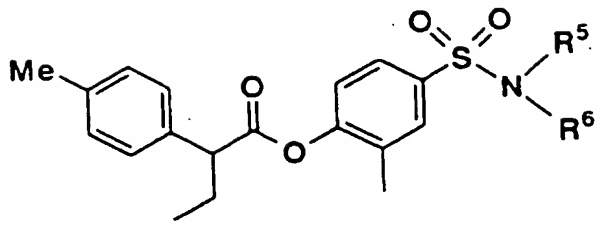
Table 20



(I-20)

No.	$(R^4)_m$	No.	$(R^4)_m$
1	Me	5	
2	Me, Me	6	
3	OMe	7	
4	OMe, OMe		

Table 21



(I-21)

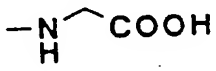
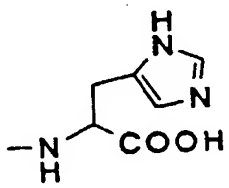
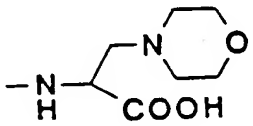
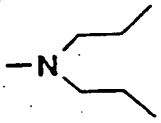
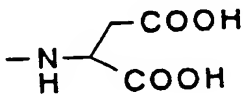
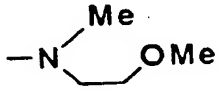
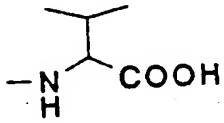
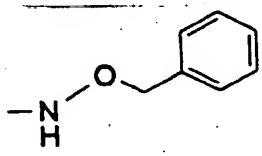
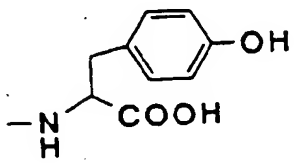
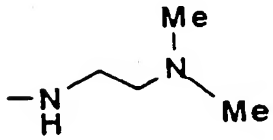
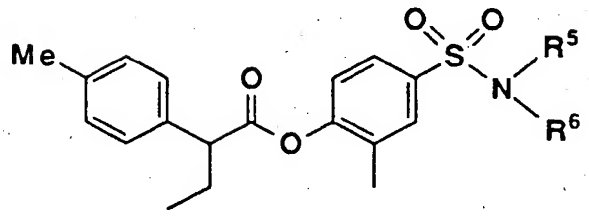
No.	$-N(R^5)(R^6)$	No.	$-N(R^5)(R^6)$
1		6	
2		7	
3		8	
4		9	
5		10	

Table 21 (continued)



(I-21)

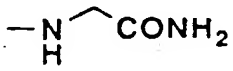
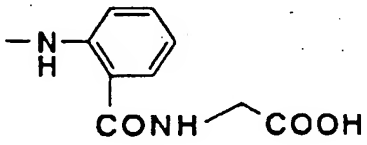
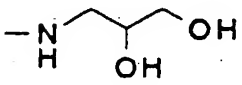
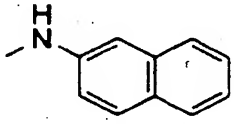
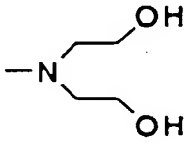
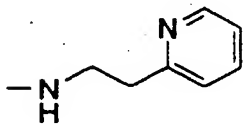
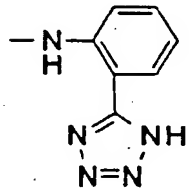
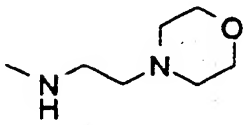
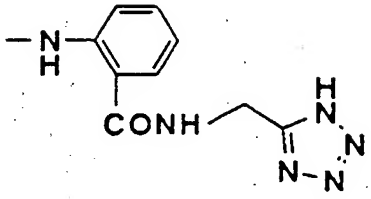
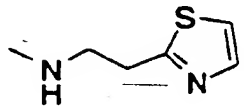
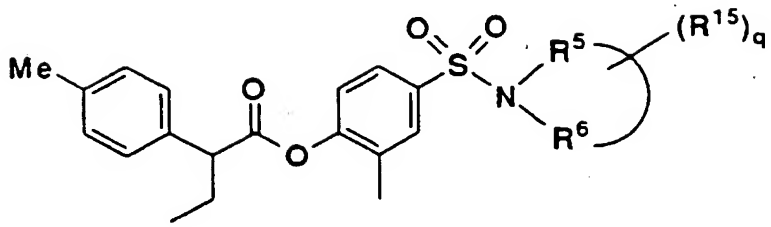
No.	$-N\begin{matrix}R^5\\R^6\end{matrix}$	No.	$-N\begin{matrix}R^5\\R^6\end{matrix}$
11		16	
12		17	
13		18	
14		19	
15		20	

Table 22



(I-22)

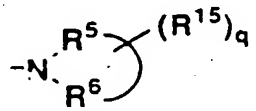
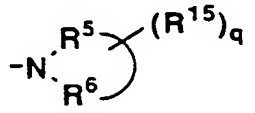
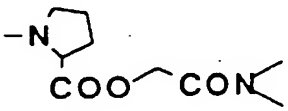
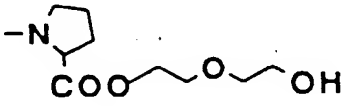
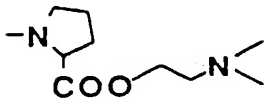
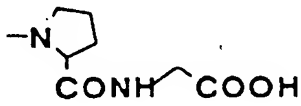
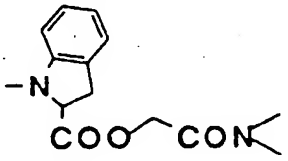
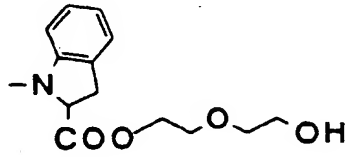
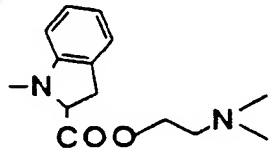
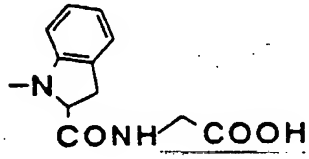
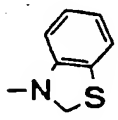
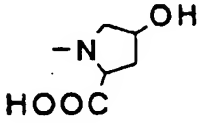
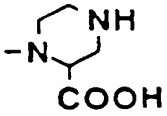
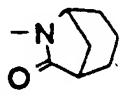
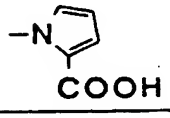
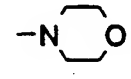
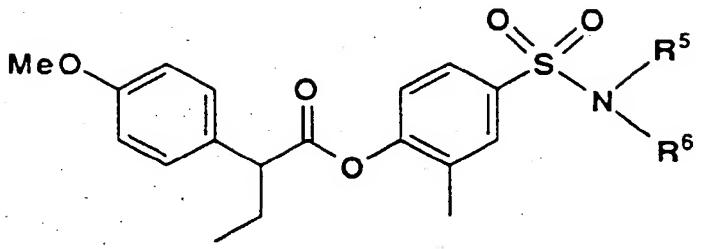
No.		No.	
1		8	
2		9	
3		10	
4		11	
5		12	
6		13	
7		14	

Table 23



(I-23)

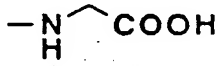
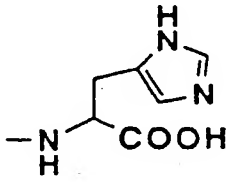
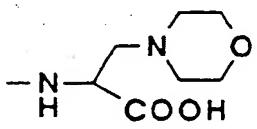
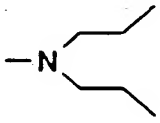
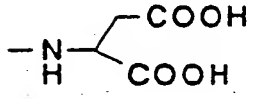
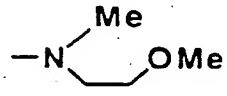
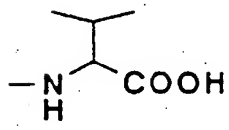
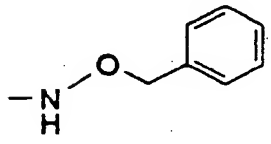
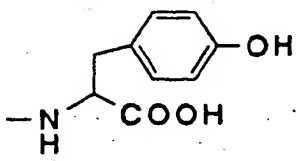
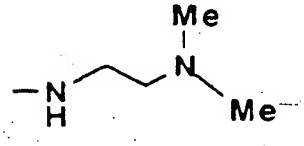
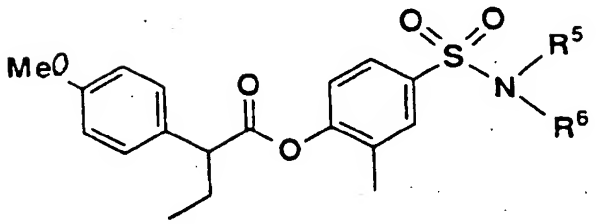
No.	$-N\begin{matrix}R^5\\R^6\end{matrix}$	No.	$-N\begin{matrix}R^5\\R^6\end{matrix}$
1		6	
2		7	
3		8	
4		9	
5		10	

Table 23 (continued)



(I-23)

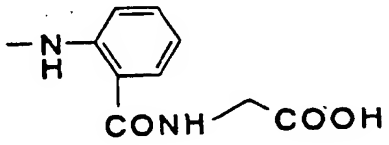
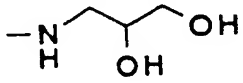
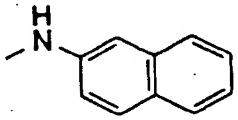
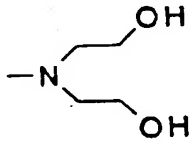
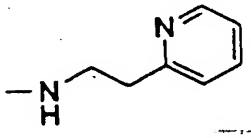
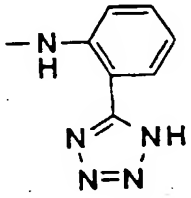
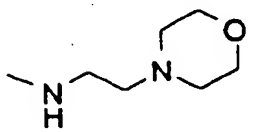
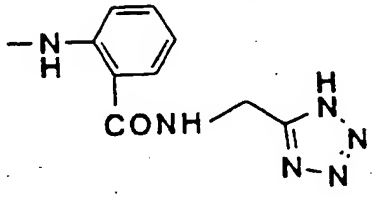
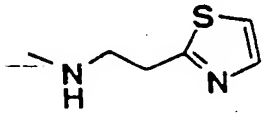
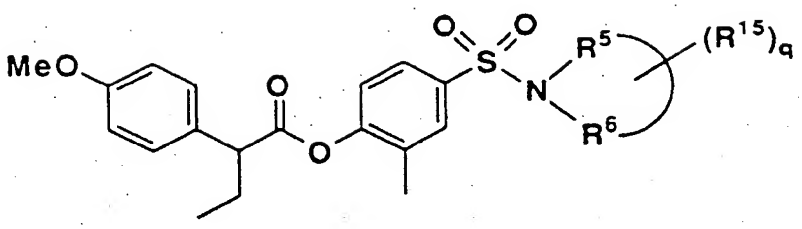
No.	$-N(R^5)(R^6)$	No.	$-N(R^5)(R^6)$
11		16	
12		17	
13		18	
14		19	
15		20	

Table 24



(I-24)

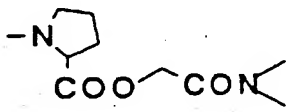
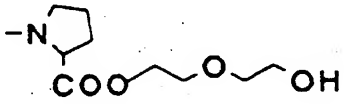
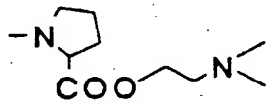
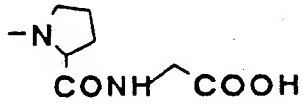
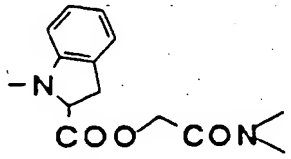
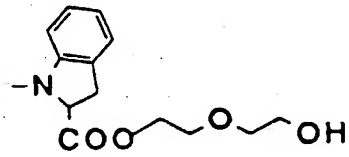
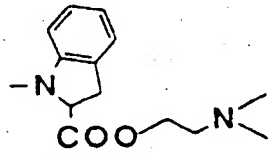
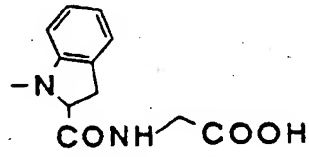
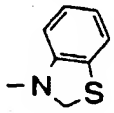
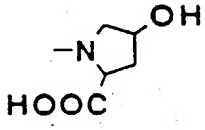
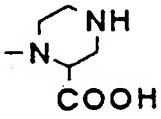
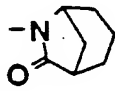
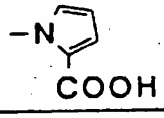
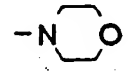
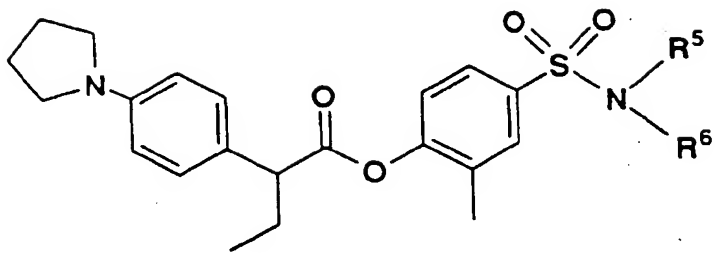
No.		No.	
1		8	
2		9	
3		10	
4		11	
5		12	
6		13	
7		14	

Table 25



(I-25)

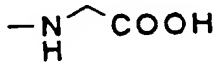
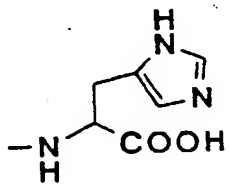
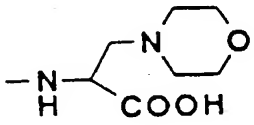
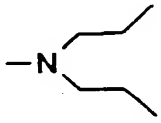
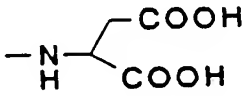
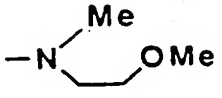
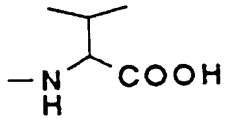
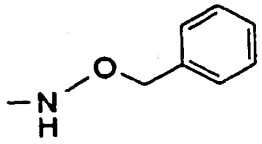
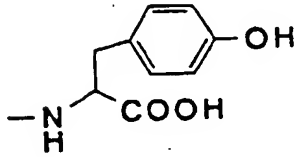
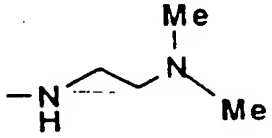
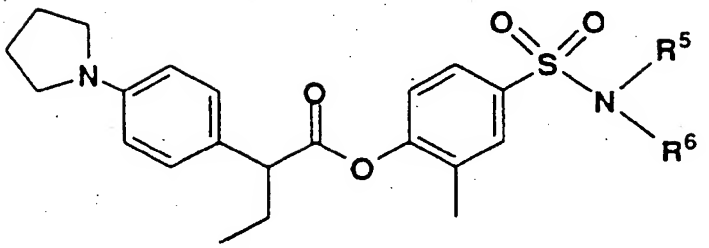
No.	$-N(R^5)(R^6)$	No.	$-N(R^5)(R^6)$
1		6	
2		7	
3		8	
4		9	
5		10	

Table 25 (continued)



(I-25)

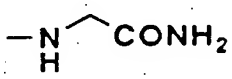
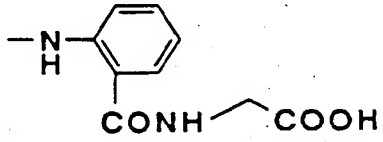
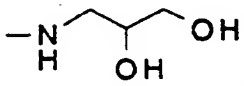
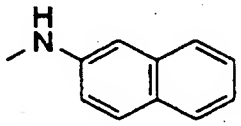
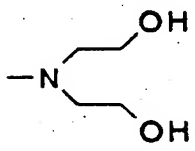
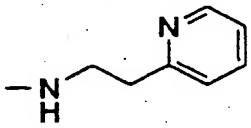
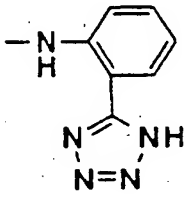
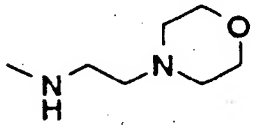
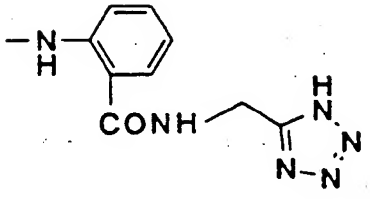
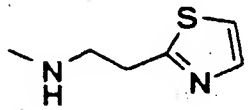
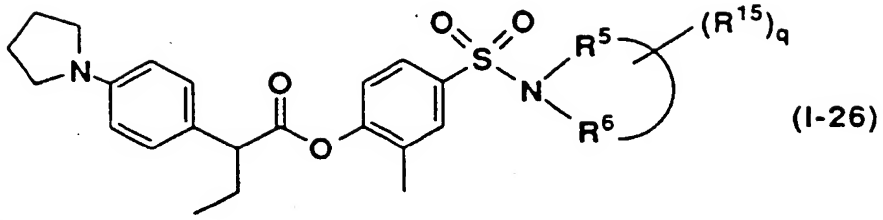
No.	$-N\begin{matrix}R^5\\R^6\end{matrix}$	No.	$-N\begin{matrix}R^5\\R^6\end{matrix}$
11		16	
12		17	
13		18	
14		19	
15		20	

Table 26



(I-26)

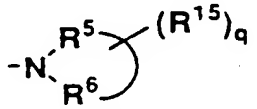
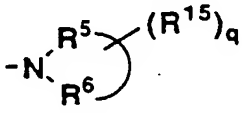
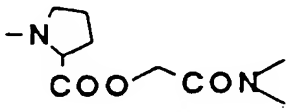
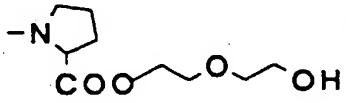
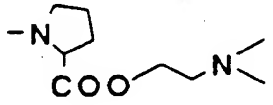
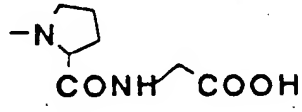
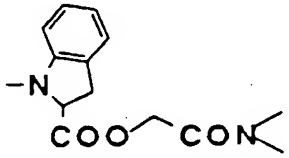
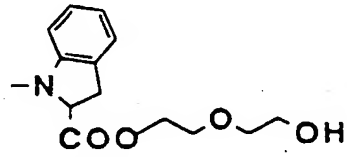
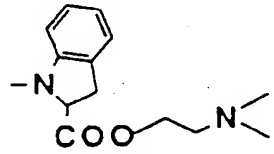
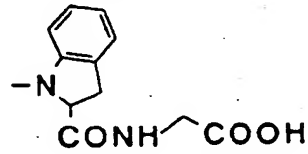
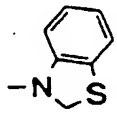
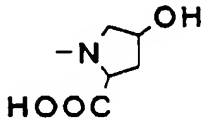
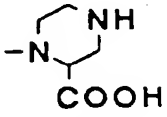
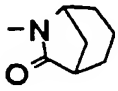
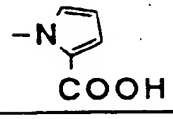
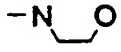
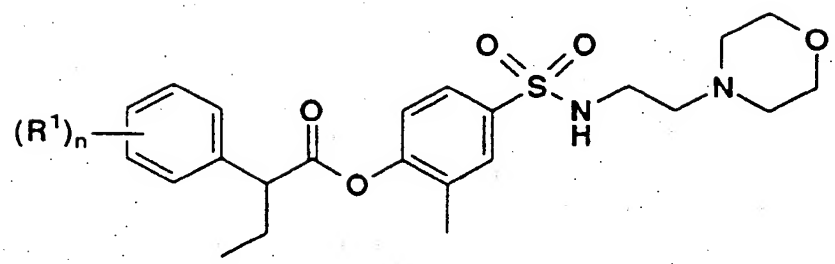
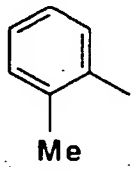
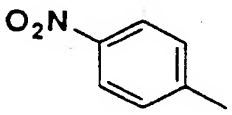
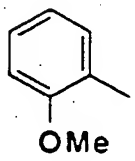
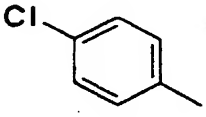
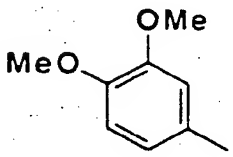
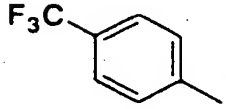
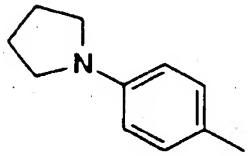
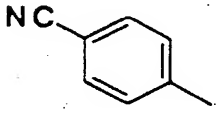
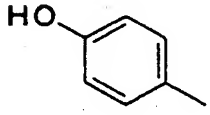
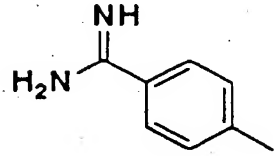
No.		No.	
1		8	
2		9	
3		10	
4		11	
5		12	
6		13	
7		14	

Table 27



(I-27)

No.	$(R^1)_n$	No.	$(R^1)_n$
1		6	
2		7	
3		8	
4		9	
5		10	

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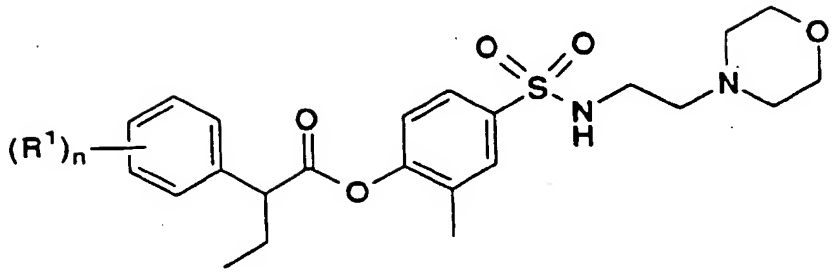


(I-27)

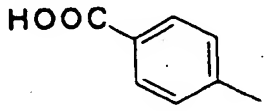
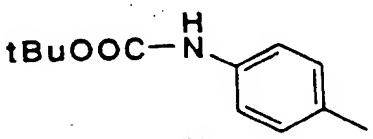
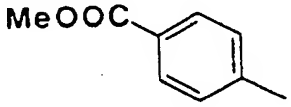
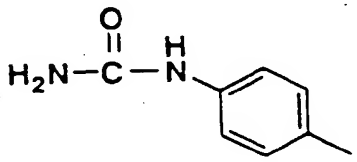
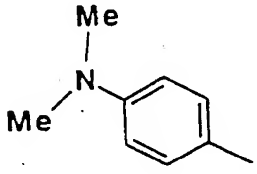
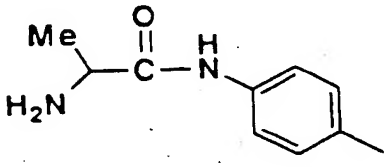
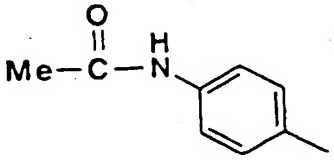
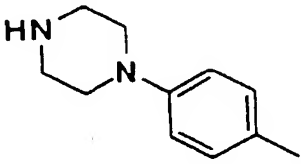
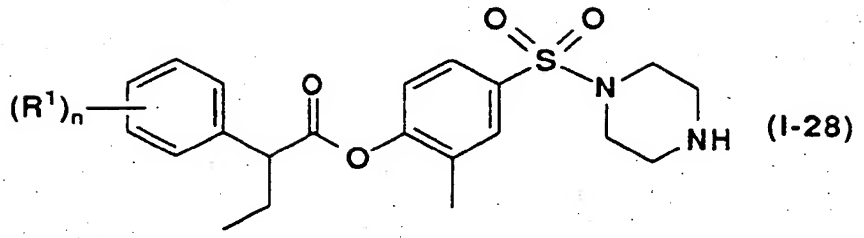
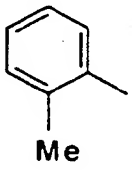
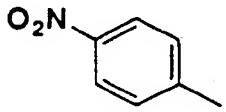
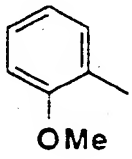
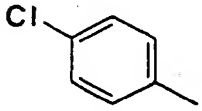
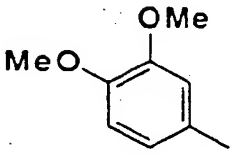
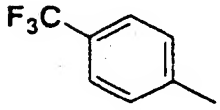
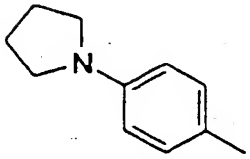
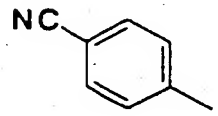
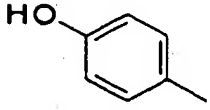
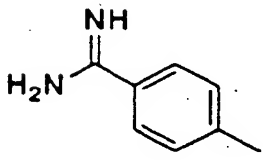
No.	$(R^1)_n$	No.	$(R^1)_n$
11		15	
12		16	
13		17	
14		18	

Table 28



(I-28)

No.	$(R^1)_n$	No.	$(R^1)_n$
1		6	
2		7	
3		8	
4		9	
5		10	

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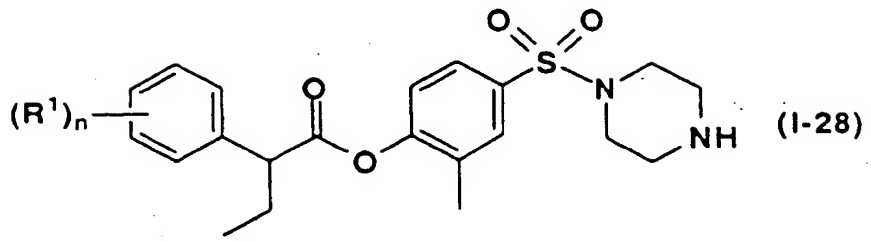


(I-28)

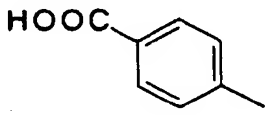
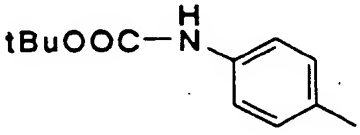
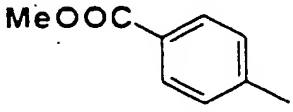
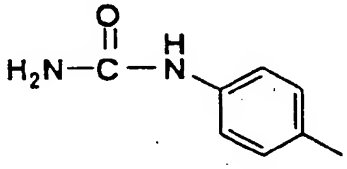
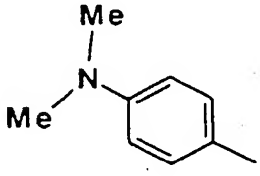
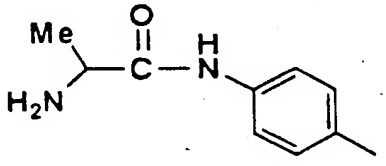
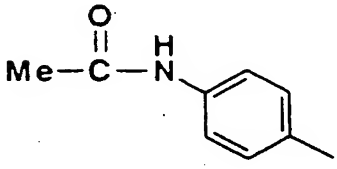
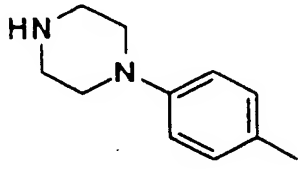
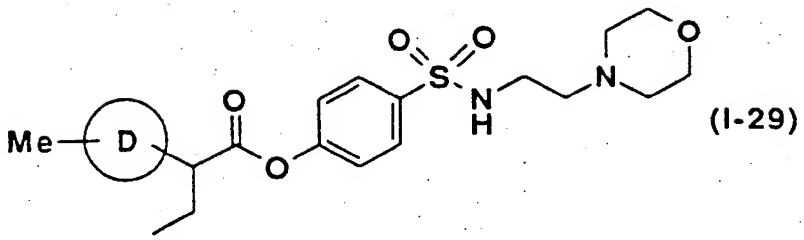
No.	$(R^1)_n$	No.	$(R^1)_n$
11		15	
12		16	
13		17	
14		18	

Table 29



(I-29)

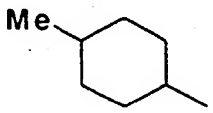
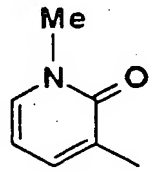
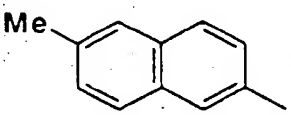
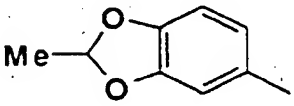
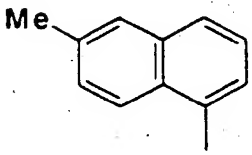
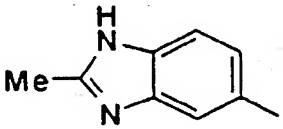
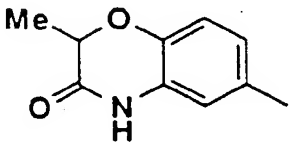
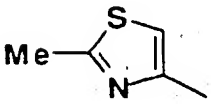
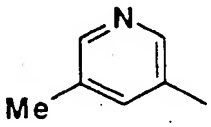
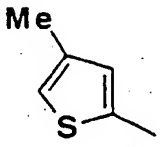
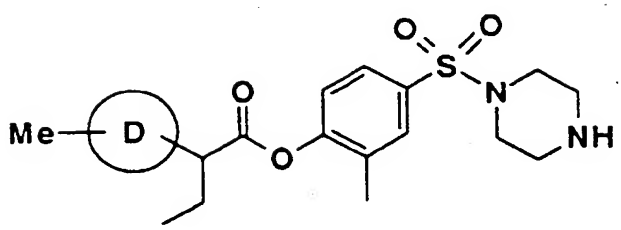
No.	Me–D–	No.	Me–D–
1		6	
2		7	
3		8	
4		9	
5		10	

Table 30



(I-30)

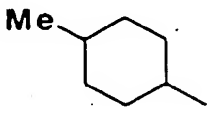
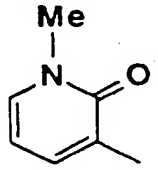
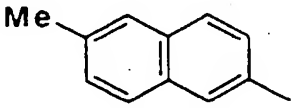
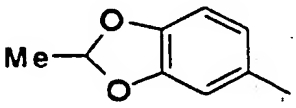
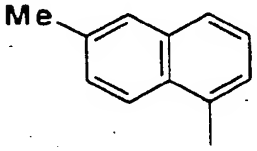
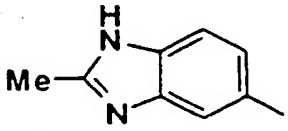
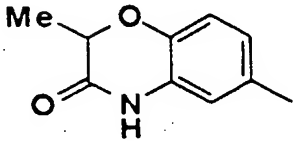
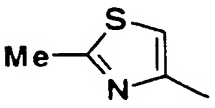
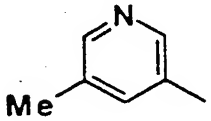
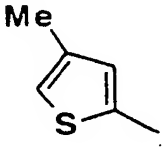
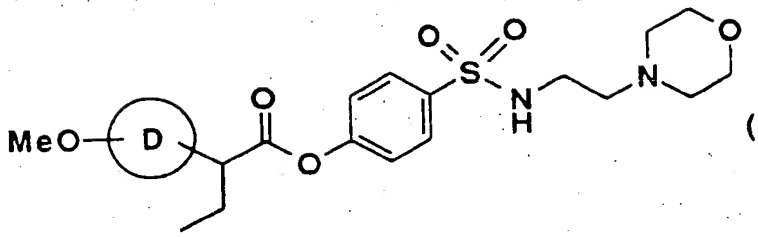
No.	Me–D–	No.	Me–D–
1		6	
2		7	
3		8	
4		9	
5		10	

Table 31



(I-31)

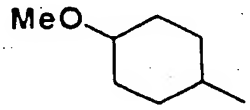
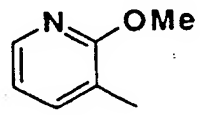
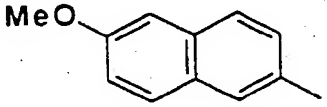
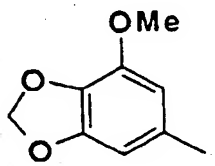
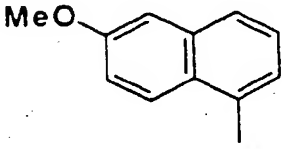
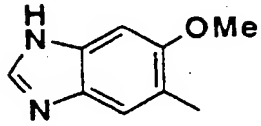
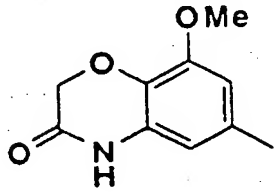
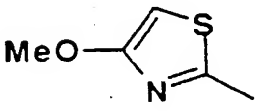
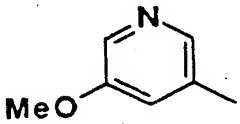
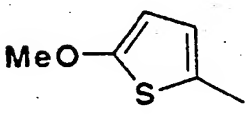
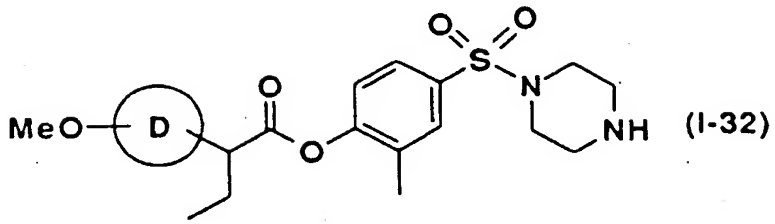
No.	MeO–D–	No.	MeO–D–
1		6	
2		7	
3		8	
4		9	
5		10	

Table 32



(I-32)

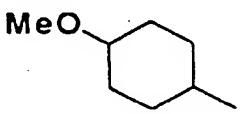
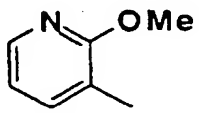
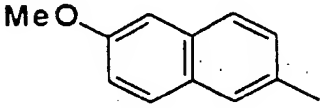
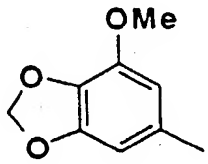
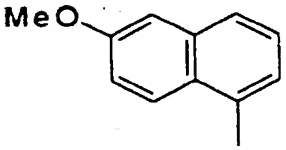
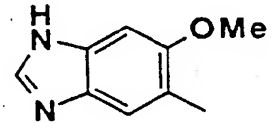
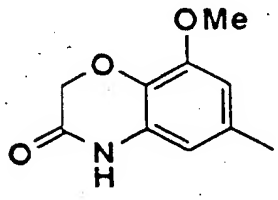
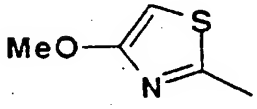
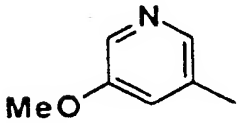
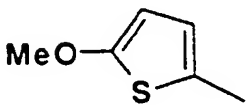
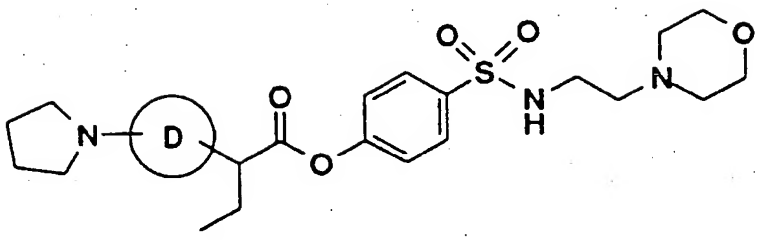
No.	MeO–D–	No.	MeO–D–
1		6	
2		7	
3		8	
4		9	
5		10	

Table 33



(I-33)

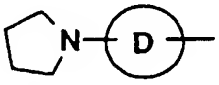
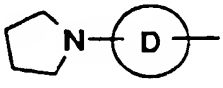
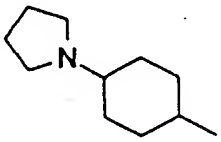
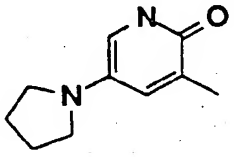
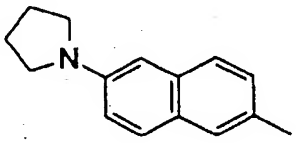
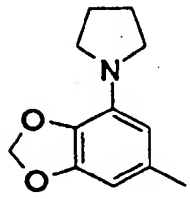
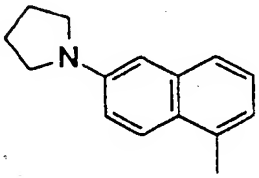
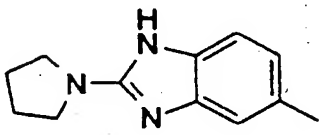
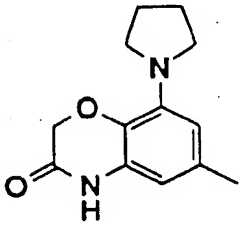
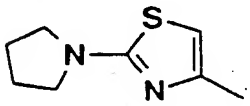
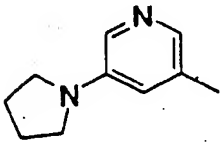
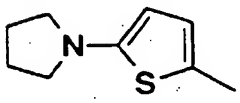
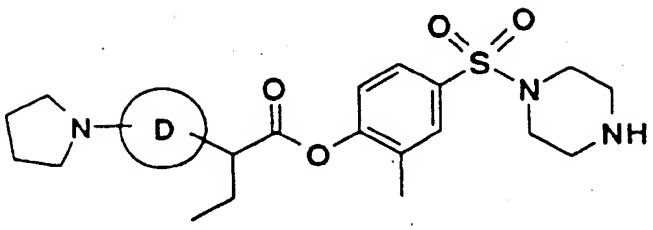
No.		No.	
1		6	
2		7	
3		8	
4		9	
5		10	

Table 34



(I-34)

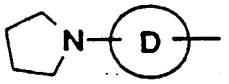
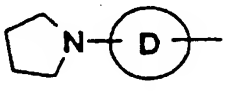
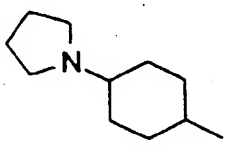
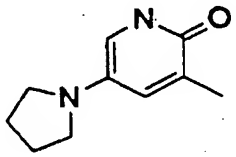
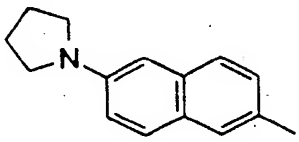
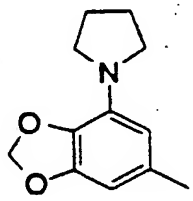
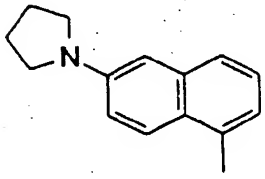
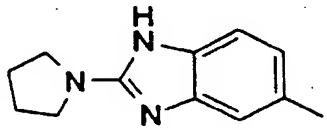
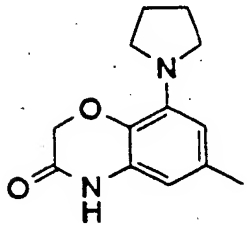
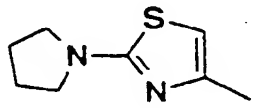
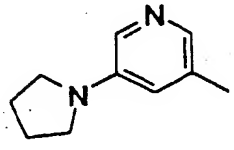
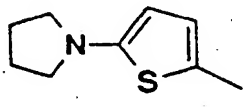
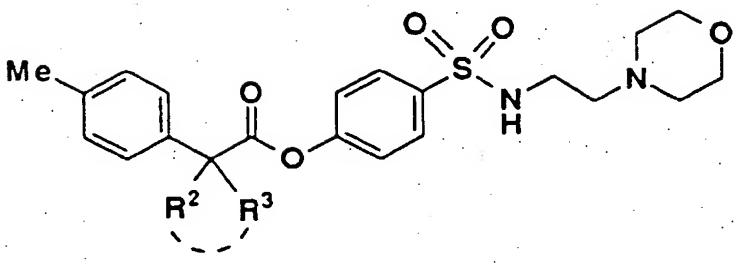
No.		No.	
1		6	
2		7	
3		8	
4		9	
5		10	

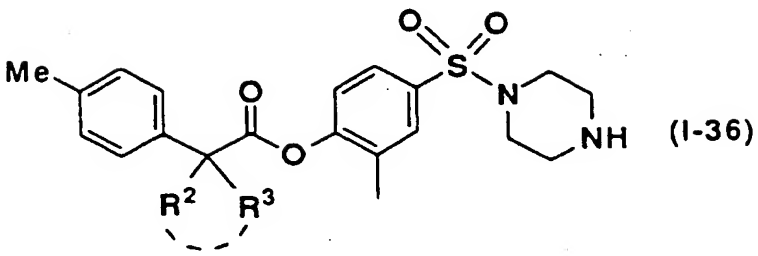
Table 35



(I-35)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

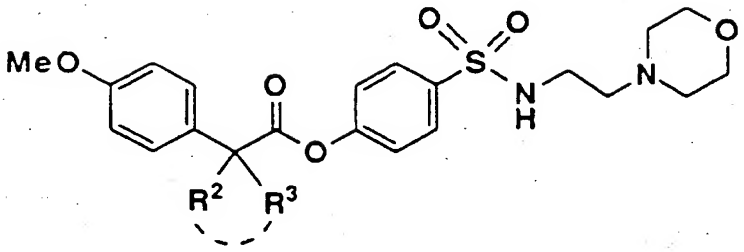
Table 36



(I-36)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

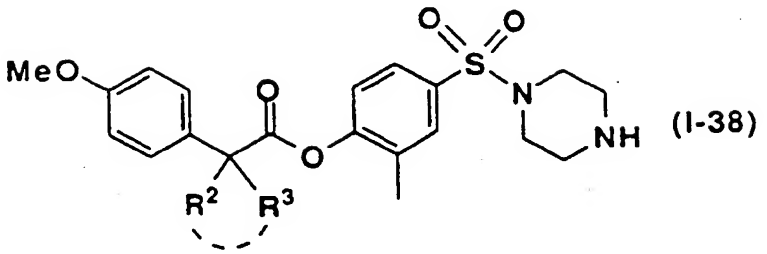
Table 37



(I-37)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

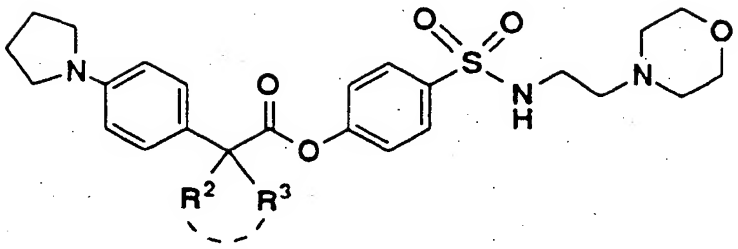
Table 38



(I-38)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

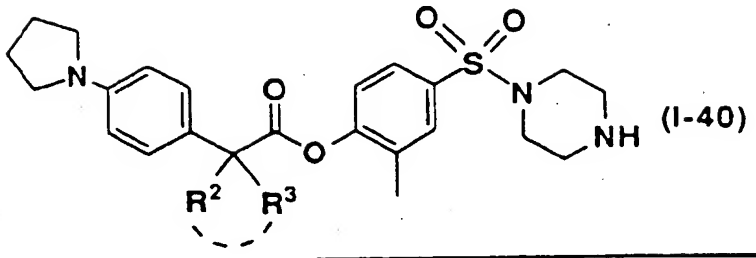
Table 39



(I-39)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

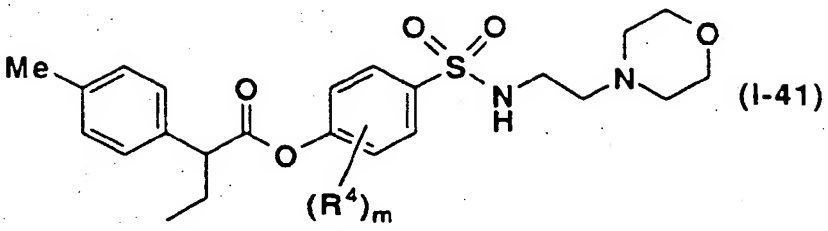
Table 40



(I-40)

No.	R^2 R^3	No.	R^2 R^3
1	H H	8	
2	Me H	9	
3	Me Me	10	
4	Et Et	11	
5	MeO H	12	Cl H
6	Pr H	13	F_3C H
7	iPr H	14	H

Table 41



(I-41)

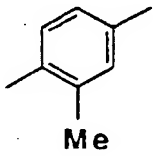
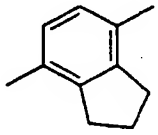
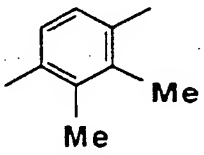
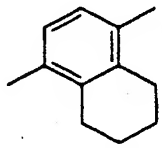
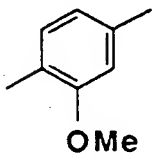
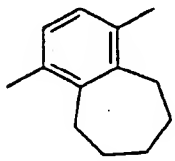
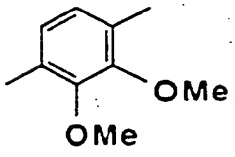
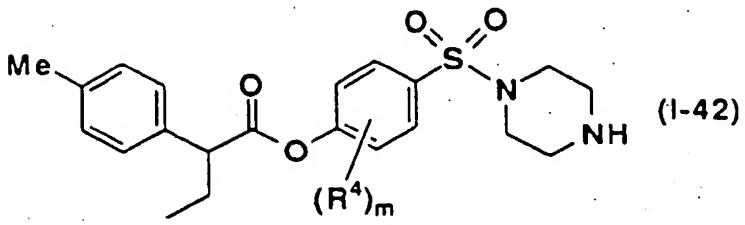
No.	$(R^4)_m$	No.	$(R^4)_m$
1		5	
2		6	
3		7	
4			

Table 42



(I-42)

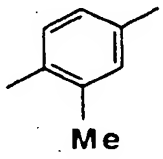
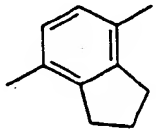
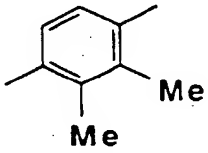
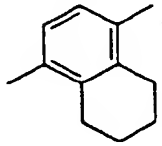
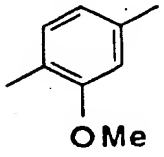
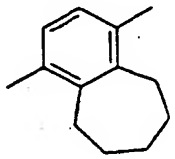
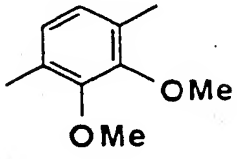
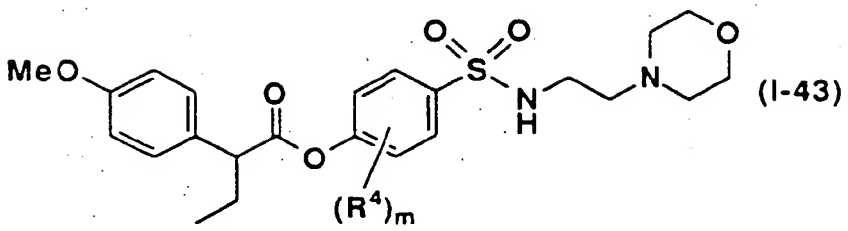
No.	$(R^4)_m$	No.	$(R^4)_m$
1		5	
2		6	
3		7	
4			

Table 43



(I-43)

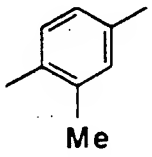
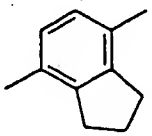
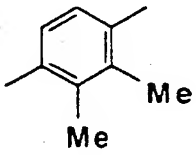
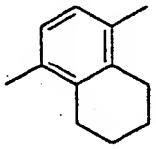
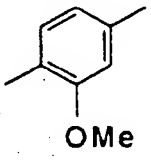
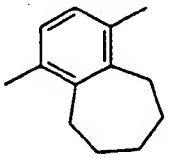
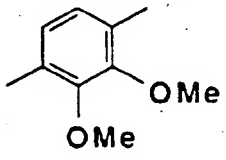
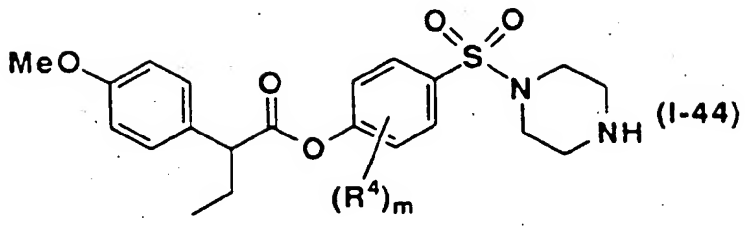
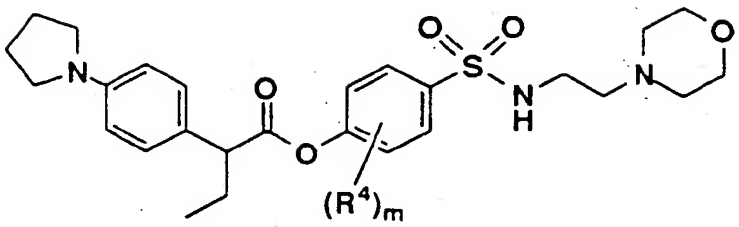
No.	$(R^4)_m$	No.	$(R^4)_m$
1		5	
2		6	
3		7	
4			

Table 44



No.	$(R^4)_m$	No.	$(R^4)_m$
1	Me	5	
2	Me, Me	6	
3	OMe	7	
4	OMe, OMe		

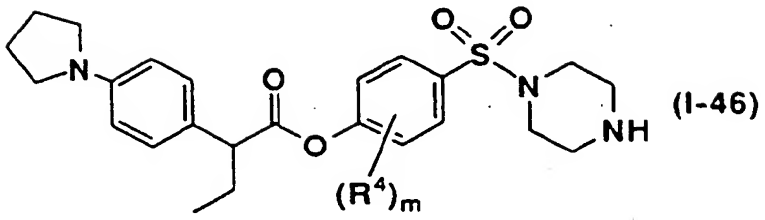
Table 45



(I-45)

No.	$(R^4)_m$	No.	$(R^4)_m$
1	Me	5	
2	Me, Me	6	
3	OMe	7	
4	OMe, OMe		

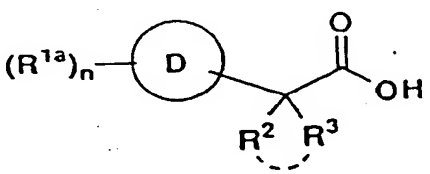
Table 46



(I-46)

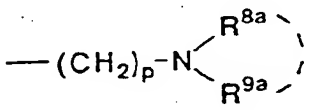
No.	$(R^4)_m$	No.	$(R^4)_m$
1	Me	5	
2	Me, Me	6	
3	OMe	7	
4	OMe, OMe		

The compounds of formula (I), of the present invention, may be prepared by esterifying a compound of formula (II)

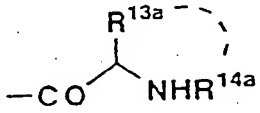


(II)

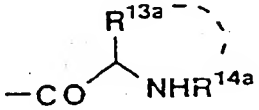
wherein R^{1a} is C1-8 alkyl, C1-8 alkoxy, hydroxy, protected hydroxy, keto, nitro, halogen atom, trihalomethyl, cyano, amidino, $-COOR^{7a}$ (in which R^{7a} is C1-8 alkyl or benzyl), or



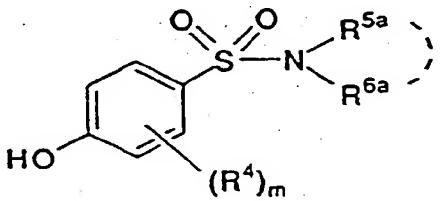
(in which p is as hereinbefore defined, R^{8a} and R^{9a} each, independently, is hydrogen atom (with the proviso that, R^{8a} and R^{9a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl, C1-4 alkyl, C2-5 acyl, $-COOR^{10a}$ (in which R^{10a} is C1-8 alkyl or benzyl), $-CONR^{11}R^{12}$ (in which R^{11} and R^{12} are as hereinbefore defined), or



(in which

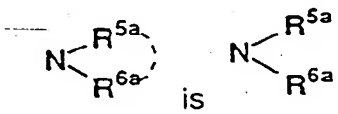


is a protected α-amino acid residue), or
R^{8a} and R^{9a}, taken together with the nitrogen atom to which they are attached represent an aliphatic heterocyclic ring which is unsubstituted or substituted by C1-4 alkyl or phenyl C1-4 alkyl, and the other symbols are as hereinbefore defined with a compound of formula (III)



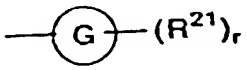
(III)

wherein

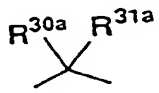


(in which R^{5a} and R^{6a} each, independently, is
1) hydrogen atom (with the proviso that, R^{5a} and R^{6a} do not represent hydrogen atom at the same time),
2) hydroxy,
3) hydroxy protected by a protecting group which is removable under acid conditions,
4) t-butoxycarbonyl,

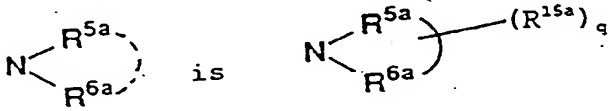
5) benzyloxycarbonyl,
6) C1-8 alkyl,
7) C1-8 alkoxy,
8) phenyl C1-4 alkoxy,
9) amidino,
10) -M-R^{16a} (in which M is as hereinbefore defined, and R^{16a} is
i) -$NR^{17a}R^{18a}$ (in which R^{17a} and R^{18a} each, independently, is hydrogen atom (with the proviso that, R^{17a} and R^{18a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), ii) -$CONR^{19}R^{20}$ (in which R^{19} and R^{20} are as hereinbefore defined),
iii)



(in which all the symbols are as hereinbefore defined), iv) heterocyclic ring, unsubstituted or substituted by 1 to 4 substituents selected from C1-4 alkyl, C1-4 alkoxy, hydroxy, phenyl C1-4 alkyl, -$COOR^{26}$ (in which R^{26} is as hereinbefore defined), hydroxy C1-4 alkyl in which hydroxy is protected by a protecting group which is removable under acid conditions or C2-4 alkoxyalkyl),
11) C1-8 alkyl substituted by one or two of -OR^{27a} (in which R^{27a} is hydrogen atom, C1-4 alkyl, C2-4 alkoxyalkyl, t-butyldimethylsilyl, THP, benzyl, or C2-4 alkyl substituted by -OH^{28a} (in which R^{28a} is hydrogen atom, C2-4 alkoxyalkyl, t-butyldimethylsilyl, THP or benzyl)),
12) -J^a-$COOR^{29}$ (in which R^{29} is as hereinbefore defined, J^a is a single bond, -$(CH_2)_s$- or



(in which s is as hereinbefore defined,
R^{30a} and R^{31a} each, independently, is i) hydrogen atom, ii) C1-8 alkyl, iii) -$COOR^{32}$ (in which R^{32} is as hereinbefore defined), iv) carbocylic or heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, amino, nitro, hydroxy, protected hydroxy, halogen atom, nitrile, guanidino and amidino, or v) C1-8 alkyl substituted by one or more substituents selected from hydroxy, protected hydroxy, -$COOR^{33}$ (in which R^{33} is as hereinbefore defined), -$NR^{34a}R^{35a}$ (in which R^{34a} and R^{35a} each, independently, is hydrogen atom (with the proviso that, R^{34a} and R^{35a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), carbocyclic or, heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, protected amino, nitro, hydroxy, protected hydroxy, halogen atom, nitrile, guanidino and amidino, with the proviso that a carbon atom of C1-8 alkyl may be replaced by a sulfur atoms, or



in which R^{5a} and R^{6a}, taken together with the nitrogen atom to which they are attached represent a heterocyclic ring,
q is as hereinbefore defined,
R^{15a} is
1) hydroxy,
2) hydroxy protected by a protecting group which is removable under acid conditions,
3) keto,
4) protected keto,
5) C1-4 alkyl,
6) C1-4 alkoxy,
7) phenyl,

8) phenoxy,
9) phenyl C1-4 alkyl,
10) phenyl C1-4 alkoxy,
11) nitro,
12) -$COOR^{36a}$ (in which R^{36a} is hydrogen atom, C1-8 alkyl, C1-4 alkyl substituted by -$CONR^{37}R^{38}$ (in which R^{37} and R^{38} are as hereinbefore defined, C1-4 alkyl substituted by -$NR^{39a}R^{40a}$ (in which R^{39a} and R^{40a} each, independently, is hydrogen atom (with the proviso that, R^{39a} and R^{40a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), C1-4 alkyl substituted by -OR^{41a} (in which R^{41a} is C2-4 alkyl substituted by -OR^{42a} (in which R^{42a} is hydrogen atom, C2-4 alkoxyalkyl or benzyl)) or C1-4 alkyl substituted by protected piperazino ring),
13)-$NR^{43a}R^{44a}$ (in which R^{43a} and R^{44a} each, independently, is hydrogen atom (with the proviso that, R^{43a} and R^{44a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl, C1-4 alkyl or C2-5 acyl),
14) -$CONR^{45a}R^{46a}$ (in which R^{45a} and R^{46a} each, independently, is hydrogen atom, C1-4 alkyl, hydroxy, hydroxy protected by a protecting group which is removable under acid conditions, phenyl C1-4 alkyloxy or C1-4 alkyl substituted by hydroxy, protected hydroxy or -$COOR^{47a}$ (in which R^{47a} is hydrogen atom, C1-8 alkyl or benzyl)),
15) C1-4 alkyl substituted by one or more substituents selected from hydroxy, protected hydroxy, -$COOR^{48a}$ (in which R^{48a} is hydrogen atom, C1-8 alkyl or benzyl), -$NR^{49a}R^{50a}$ (in which R^{49a} and R^{50a} each, independently, is hydrogen atom (with the proviso that, R^{49a} and R^{50a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), or 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,
16) 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,
17) halogen atom,
18) -CHO protected by a protecting group which is removable under acid conditions, or
19) -NR^{51a}-$COOR^{52a}$ (in which R^{51a} and R^{52a} each, independently, is hydrogen atom or C1-8 alkyl), and the other symbols are as hereinbefore defined , or

may be prepared by esterifying a compound of formula (II) with a compound of formula (III) to obtain a compound having protected group(s) and then eliminating the protecting group(s) (e.g.by hydrolysis of t-butylester, treatment with acid and/or hydrogenolysis), or may be prepared by esterifying a compound of formula (II) with a compound of formula (III), if necessary, eliminating the protecting groups to obtain a compound having R^{15} represent C1-4 alkyl substituted by hydroxy, and then subjecting to sulfuric acid esterification; and optionally converting a compound of formula (I) thus obtained into a non-toxic salt, acid addition salt or solvate thereof.

Protected hydroxy means, for example, hydroxy protected by a protecting group which is removable under acid conditions (e.g. C2-4 alkoxyalkyl, t-butyldimethylsilyl, tetrahydropyran (THP), triphenylmethyl) or hydroxy protected by a protecting group which is removable by hydrogenation (e.g. benzyl).

Hydroxy protected by a protecting group which is removable under acid conditions means, for example, hydroxy group protected by C2-4 alkoxyalkyl, t-butyldimethylsilyl, tetrahydropyran (THP) or triphenylmethyl.

Protected amino acid, α-amino acid or piperazino ring means, for example, amino acid, α-amino acid or piperazino ring protected by t-butoxycarbonyl (Boc) or benzyloxycarbonyl (Cbz).

-CHO protected by a protecting group which is removable under acid conditions means, for example, -CHO protected by acetal (e.g. dimethylacetal or diethylacetal or ketal (e.g. ethylenedioxyketal or trimethylenedioxyketal).

The above esterification is known *per se* and can be carried out by methods for example:

(1) using an acid halide,
(2) using a mixed acid anhydride,
(3) using a condensing agent.

Each of these methods can be carried out, for example, as follows:

(1) the method using an acid halide may be carried out, for example, by reacting a carboxylic acid with an acid halide (e.g., oxalyl chloride or thionyl chloride) in an inert organic solvent (e.g., chloroform, methylene chloride, diethyl ether or tetrahydrofuran) or without a solvent at from -20°C to the reflux temperature of the solvent, and then by reacting the acid halide obtained with a corresponding alcohol in the presence of a tertiary amine (e.g. pyridine, triethylamine, dimethylaniline or dimethylaminopyridine) in an inert organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran), at a temperature of from 0°C to 40°C.

(2) the method using a mixed acid anhydride may be carried out, for example, by reacting a carboxylic acid and an acid halide (e.g. pivaloyl chloride, tosyl chloride or mesyl chloride) or an acid derivative (e.g. ethyl chloroformate or isobutyl chloroformate) in the presence of a tertiary amine (e.g. pyridine, triethylamine, dimethylaniline or dimethylaminopyridine) in an inert organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran)

or without a solvent at a temperature of from 0°C to 40°C, and then by reacting the mixture of acid anhydride obtained with a corresponding alcohol in an inert organic solvent (e.g. chloroform, methylene chloride, diethyl ether or tetrahydrofuran), at a temperature of from 0°C to 40°C,

(3) the method using a condensing agent (e.g., 1,3-dicyclohexyl carbodiimide (DCC), 1-ethyl-3-[3-(dimethylamino) propyl]carbodiimide (EDC) or 2-chloro-1-methylpyridinium iodide) may be carried out, for example, by reacting a carboxylic acid with a corresponding alcohol using a condensing agent in the presence or absence of a tertiary amine (e.g. pyridine, triethylamine, dimethylaniline or dimethylaminopyridine) in an inert organic solvent (e.g., chloroform, methylene chloride, dimethyl formamide or diethyl ether) or without a solvent at a temperature of from 0°C to 40°C.

The reactions (1), (2) and (3) hereinbefore described may be preferably carried out in an atmosphere of inert gas (e.g. argon or nitrogen) under anhydrous conditions.

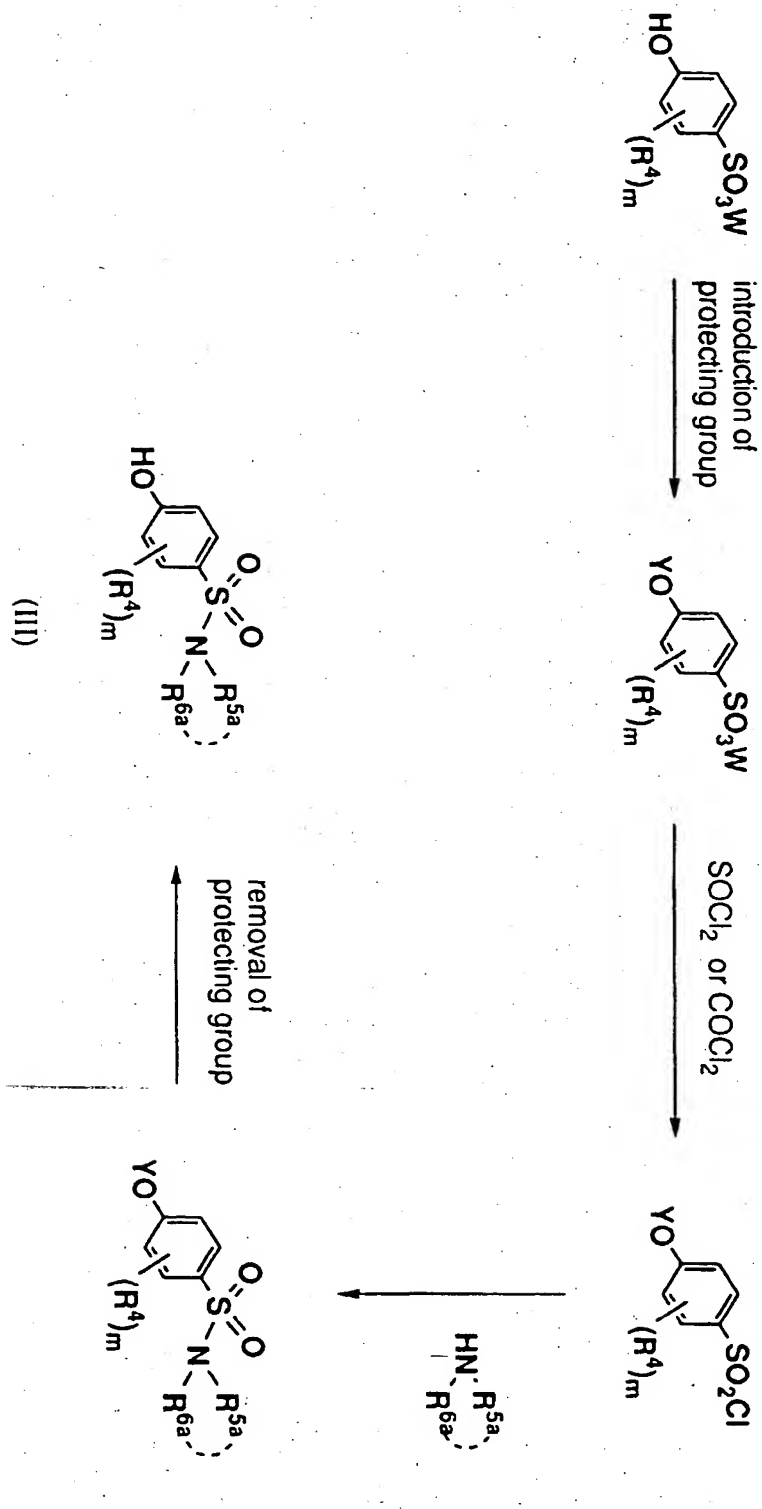
The hydrolysis of t-butylester group or the reaction resulting from treatment with acid (e.g. elimination of C2-4 alkoxyalkyl, t-butoxycarbonyl or dimethylacetal) is known *per se* and may be carried out, for example, by using an organic acid (e.g. trifluoroacetic acid) or an inorganic acid (e.g. hydrochloric acid), or a mixture thereof, in an inert organic solvent (e.g. methylene chloride, chloroform, methanol, dioxane, ethyl acetate or anisole) at a temperature of from 0°C to 90°C.

The hydrogenolysis is known *per se*, and may be carried out, for example, in an inert solvent [such as an ether (e.g. tetrahydrofuran, dioxane, diethoxyethane or diethyl ether), an alcohol (e.g., methanol or ethanol), a benzene analogue (e.g. benzene or toluene), a ketone (e.g. acetone or methyl ethyl ketone), a nitrile (e.g. acetonitrile), an amine (e.g. dimethylformamide), water, ethyl acetate, acetic acid or a mixture of two or more of them], in the presence of a hydrogenation catalyst (e.g., palladium on activated carbon, palladium black, palladium, palladium hydroxide on carbon, platinum oxide, nickel or Raney nickel (registered trade mark)), in the presence or absence of an inorganic acid (e.g. hydrochloric acid, sulfuric acid, hypochlorous acid, boric acid or tetrafluoroboric acid) or an organic acid (e.g., acetic acid, p-toluenesulfonic acid, oxalic acid, trifluoroacetic acid or formic acid), at ordinary or elevated pressure under an atmosphere of hydrogen, at a temperature of from 0°C to 200°C. When using an acid, its salt may be used at the same time.

The sulfuric acid esterification is known *per se*, and may be carried out, for example, by reacting sulfur trioxide pyridine complex in the presence of a tertiary amine (e.g. pyridine) at a temperature of from 0°C to 40°C.

The compounds of formulae (II) and (III) used as starting materials may be prepared by the methods of the following Scheme 1 or by methods known *per se* or are commercially available compounds. For example, 2-phenylbutanoic acid is commercially available. The compounds may also be prepared by the methods described in the Examples of the present specification.

Scheme 1



In Scheme 1 hereinbefore described

W is an alkali metal,

Y is benzyl, benzyloxycarbonyl, or a protecting group which may be removed under acid conditions (e.g. C2-4 alkoxyalkyl, t-butyldimethylsilyl, tetrahydropyran (THP) or triphenylmethyl), and
the other symbols are as hereinbefore defined.

It has been confirmed that the compounds of the formula (I), of the present invention have inhibitory activities on elastase. For example, in laboratory tests the following results were obtained.

(1) Inhibitory effects on human polymorphonuclear elastase

A mixture with 0.5 ml of 0.2 mM HEPES buffer (pH 8.0), 0.2 ml of 2.5 M NaCl, 0.1 ml of 1 % polyethyleneglycol 6000, 0.13 ml of distilled water, test compound dissolved in 0.01 ml of dimethylsulfoxide (DMSO) and 0.05 ml of 0.8 Unit/ml human polymorphonuclear elastase (HSE) was preincubated at 37 °C for 20 min. 5 mM of Meo-Suc-Ala-Ala-Pro-Val-pNA (DMSO solution, 0.01ml) was then added to the above mixture and was incubated at 37°C for 5 min. The reaction was terminated by 0.1 ml of 50% acetic acid and the p-nitroanilide (pNA) released was measured spectrophotometrically at 405 nM. Percent inhibition of a compound was calculated by the following equation.

$$\text{Inhibition (\%)} = 1-\{\text{delta OD(test-blank)/delta OD(control-blank)}\}\times 100$$

Results are shown in Table 47.

[Table 47]

Example No.	IC_{50} (μM)
1(16)	0.017
1(40)	0.019
1(56)	0.014
1(78)	0.0080
1(130)	0.022
1(139)	0.024
2	0.055
2(1)	0.012
2(42)	0.013
2(62)	0.0068
2(69)	0.011
2(77)	0.018
2(111)	0.0097
2(120)	0.023
2(157)	0.008
2(173)	0.014
2(179)	0.049
2(197)	0.010
2(274)	0.012
2(276)	0.0093

(2) Inhibitory effects on human polymorphonuclear elastase induced lung hemorrhage in hamster

A test compound suspended in 0.5 % Carboxymethylcellulose or 80 % Polyethyleneglycol, 400 or 2 % Tween 80 was administered orally to a group of 5 Syrian hamsters. At 60 min after the administration, 10 U/0.1 ml of HSE was injected intratracheally via surgically exposed trachea under pentobarbital anesthesia (60 mg/kg, i.p.) to induce lung injury. At 60 min after the injection, hamsters were bled to sacrifice and subjected to bronchoalveolar lavage with 2.5 ml of saline and recovered lavage solution (BALF). The recovered BALF (0.5 ml) was diluted by 4 times with 2 % aqueous solution sodium carbonate and sonicated for 10 sec. The lavage fluid was further diluted by 2.5 times with 2% aqueous solution sodium carbonate and the amount of blood in BALF was calculated from absorbance at 414 nM using standard curve.

Results are shown in Table 48 and 49.

[Table 48]

Example No.	inhibition at 500 mg/kg (%)
1(68)	51
1(90)	65
2	81
2(42)	67
2(69)	83

[Table 49]

Example No.	ED_{50}
1(139)	192 mg/kg
2(274)	132 mg/kg
2(276)	73 mg/kg

The above experiments show that compounds of the present invention possess inhibitory activity on elastase, even when administered orally.

The toxicity of the compounds of the present invention is very low. Therefore, the compounds of the present invention may be considered to be sufficiently safe and suitable for pharmaceutical use.

The compounds of the formula (I), of the present invention, and non-toxic salts and acid addition salts thereof, possess inhibitory activity on elastase. Accordingly, they are useful for the treatment and/or prevention of diseases induced by an abnormal enhancement of the degradation of elastin, collagen fiber and/or proteoglycan, resulting from the action of elastase on a mammalian animal, especially a human (e.g. chronic obstructive pulmonary disease such as emphysema, rheumatoid arthritis, atherosclerosis, adult respiratory distress syndrome (ARDS), glomerular nephritis, myocardial infarction, idiopathic ulcerative colitis or gingivitis).

For the purpose above described, the compounds of the formula (I), of the present invention, or non-toxic salts, acid addition salts or solvates thereof may normally be administered systemically or locally usually by oral or parenteral administration.

The doses to be administered are determined depending upon, for example, age, body weight, symptom, the desired therapeutic effect, the route of administration, and the duration of the treatment. In the human adult, the doses per person are generally from 1 mg to 1000 mg, by oral administration, up to several times per day, or from 0.1 mg to 100 mg, by parenteral administration up to several times per day, or by continuous administration for from 1 to 24 hrs. per day from vein.

As mentioned above, the doses to be used depend upon various conditions. Therefore, there are cases in which doses lower than or greater than the ranges specified above may be used.

The compounds of the present invention may be administered in the form of, for example, solid compositions, liquid compositions or other compositions for oral administration, injections, liniments or suppositories for parenteral administration.

Solid compositions for oral administration include compressed tablets, pills, capsules, dispersible powders, and granules. Capsules include hard capsules and soft capsules.

In such compositions, one or more of the active compound(s) may be admixed with at least one inert diluent (such as lactose, mannitol, glucose, hydroxypropyl cellulose, microcrystalline cellulose, starch, polyvinylpyrrolidone or magnesium metasilicate aluminate). The compositions may also comprise, as is normal practice, additional substances other than inert diluents: e.g. lubricating agents (such as magnesium stearate), disintegrating agents (such as cellulose calcium glycolate), stabilizing agents (such as lactose), and agents to assist dissolution (such as glutamic acid or asparaginic acid).

The tablets or pills may, if desired, be coated with a film of gastric or enteric material (such as sugar, gelatin, hydroxypropyl cellulose or hydroxypropylmethyl cellulose phthalate), or be coated with two or more films. And further, coating may include containment within capsules of absorbable materials such as gelatin.

Liquid compositions for oral administration include pharmaceutically-acceptable solutions, emulsions, suspensions, syrups and elixirs. In such compositions, one or more of the active compound(s) contained in inert diluent(s) commonly used in the art (e.g. purified water or ethanol). Besides inert diluents, such compositions may also comprise adjuvants (such as wetting agents or suspending agents, sweetening agents, flavouring agents, perfuming agents, and preserving agents.

Other compositions for oral administration include spray compositions which may be prepared by known methods and which comprise one or more of the active compound(s). Spray compositions may comprise additional substances other than inert diluents: e.g. stabilizing agents (such as sodium sulfate), isotonic buffers (such as sodium chloride, sodium citrate or citric acid). For preparation of such spray compositions, for example, the method described in the United States Patent No. 2868691 or 3095355 may be used.

Injections for parenteral administration include sterile aqueous or non aqueous solutions, suspensions and emulsions. In such compositions, one or more active compound(s) may be admixed with at least one inert aqueous diluent (s) (e.g. distilled water for injection or physiological salt solution) or inert non-aqueous diluent(s) (e.g. propylene glycol, polyethylene glycol, olive oil, ethanol or POLYSORBATE80 (registered trade mark).

Injections may comprise additional ingredients other than inert diluents: e.g. preserving agents, wetting agents, emulsifying agents, dispersing agents, stabilizing agents (e.g. lactose), assisting agents such as agents to assist dissolution (e.g. glutamic acid or asparaginic acid).

They may be sterilized for example, by filtration through a bacteria-retaining filter, by incorporation of sterilizing agents in the compositions or by irradiation. They may also be manufactured in the form of sterile solid compositions, for example, by freeze-drying, which may be dissolved in sterile water or some other sterile diluent(s) for injection immediately before used.

Other compositions for parenteral administration include liquids for external use, and endermic liniments, ointment, suppositories and pessaries which comprise one or more of the active compound(s) and may be prepared by methods known *per se*.

Reference examples and Examples

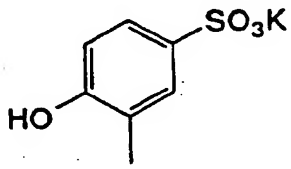
The following reference examples and examples illustrate, but do not limit, the present invention.

The solvents in parentheses show the developing or eluting solvents and the ratios of the solvents used are by volume in chromatographic separations and TLC.

The NMR data show the solvents used in the measurements in parentheses.

Reference example 1

3-methyl-4-hydroxybenzenesulfonic acid • potassium salt

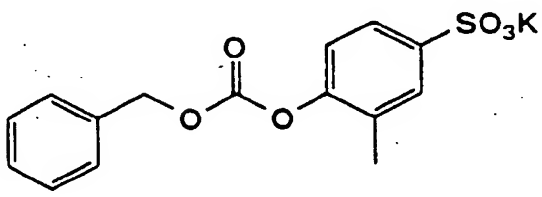


To stirring conc. sulfuric acid (26 ml) at 100 °C was slowly added o-cresol (50 ml), the mixture was stirred at 100 °C for 5 hours. After the reaction mixture was cooled at room temperature, to mixture was neutralized by slowly adding potassium hydroxide (27.5 g) in water (35 ml) solution. After to the mixture was added methanol (100 ml), the precipitate was filtered to give the title compound (56.5 g) having the following physical data.

TLC : Rf 0.18 (chloroform:methanol:water=6:4:1).

Reference example 2

3-methyl-4-(benzyloxycarbonyloxy)benzenesulfonic acid • potassium salt

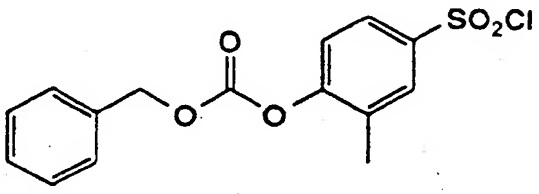


To a suspension of the compound prepared in reference example 1 (12.2 g) in tetrahydrofuran (THF) (100 ml) was added 2N aqueous solution of sodium hydroxide (28 ml) at room temperature, following added benzyloxycarbonyl chloride (8 ml) under cooling with ice. The reaction mixture was stirred for 30 min. The reaction mixture was concentrated under reduced pressure, and cooled with ice, and the precipitate was filtered to give the title compound (7.3 g) having the following physical data.

TLC : Rf 0.51 (chloroform:methanol:water=6:4:1).

Reference example 3

3-methyl-4-(benzyloxycarbonyloxy)benzenesulfonyl chloride

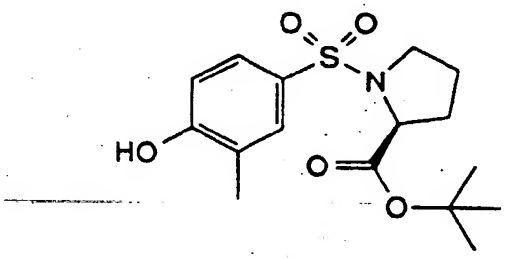


To a suspension of the compound prepared in reference example 2 (46.1 g) in dimethylformamide (DMF) (100 ml) was slowly added thionyl chloride (15 ml) under cooling with ice. The reaction mixture was stirred for 30 min at 5 °C. To the reaction mixture was added ice water, and the precipitate was filtered to give the title compound (39.4 g) having the following physical data.

TLC : Rf 0.56 (chloroform:methanol:water=6:4:1).

Reference example 4

4-(2S-t-butyloxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenol

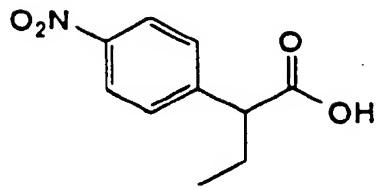


To a solution of L-proline-t-butylester (1.9 g) in pyridine (10 ml) was added the compound prepared in reference example 3 (3.7 g) under cooling with ice. The reaction mixture was stirred for 30 min. The mixture was quenched by adding 2N aqueous solution hydrochloric acid and extracted with ethyl acetate (200 ml). The organic layer was washed with a saturated aqueous solution of sodium hydrocarbonate and a saturated aqueous solution of sodium chloride, dried over anhydrous magnesium sulfate and concentrated. 10 % Palladium on activated carbon (500 mg) was added to a solution of the residue (4.9 g) in methanol (200 ml) and the mixture was stirred for 2 h at room temperature under an atmosphere of hydrogen. The mixture was filtered through Celite (being on sale). The filtrate was concentrated to give the tittle compound (3.4 g) having the following physical data.

TLC : Rf 0.35 (hexane:ethyl acetate=1:1).

Reference example 5

2RS-(4-nitrophenyl)butanoic acid

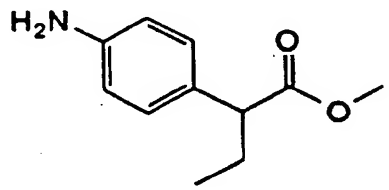


To a mixture solution of 2-phenylbutanoic acid (200 g) in acetic acid (200 ml) and conc. sulfuric acid (150 ml) was slowly added conc. nitric acid (150 ml) at 15 °C. The reaction mixture was stirred for 10 min at same temperature. The reaction mixture was poured into ice water, and the precipitate was filtered. The residue was recrystallized from the mixture solution of hexane/ethyl acetate to give the title compound (103 g) having the following physical data.

TLC : Rf 0.50 (ethyl acetate).

Reference example 6

2RS-(4-aminophenyl)butanoic acid methylester

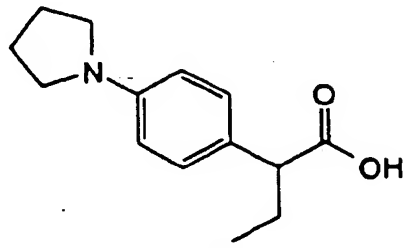


To a solution of the compound prepared in reference example 5 (15.7 g) in DMF (60 ml) was added potassium carbonate (12 g) under cooling with ice. To the mixture was added methyl iodide (5 ml) at same temperature. The reaction mixture was stirred for 2h at room temperature. The mixture was quenched by adding 1N aqueous solution hydrochloric acid (200 ml) and extracted with the mixture of hexane/ethyl acetate (1:1, 200 ml). The organic layer was washed with water and a saturated aqueous solution of sodium chloride, dried over anhydrous magnesium sulfate and concentrated. 5 % Palladium on activated carbon (1.3 g) was added to a solution of the residue in methanol (300 ml) and the mixture was stirred for 2 h at room temperature under an atmosphere of hydrogen. The mixture was filtered through Celite (being on sale). The filtrate was concentrated to give the tittle compound (14.2 g) having the following physical data.

TLC : Rf 0.47 (hexane:ethyl acetate=1:1).

Reference example 7

2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid



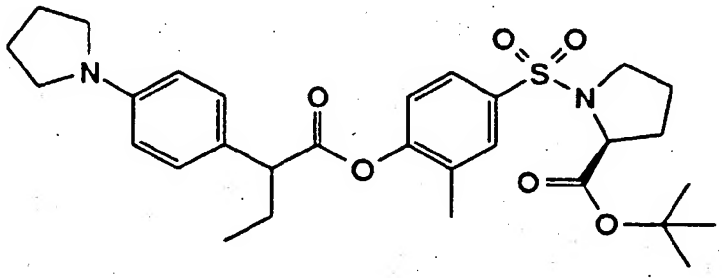
To a solution of the compound prepared in reference example 6 (14.2 g) in DMSO (75 ml) was added potassium carbonate (11 g) and 1,4-dibromobutane (9 ml). The reaction mixture was stirred for 1h at 40°C. To the mixture was

added sodium iodide (11.2 g). the reaction mixture was stirred for 3h at 40 °C and stirred for 2h at 60 °C. The reaction mixture was quenched by adding water and extracted with the mixture of hexane/ethyl acetate (1:1, 1000 ml). The organic layer was washed with water and a saturated aqueous solution of sodium chloride, dried over anhydrous magnesium sulfate and concentrated. To a solution of the residue in methanol (80 ml) was added 5N aqueous solution of sodium hydroxide (20 ml) and the mixture was stirred for 5 h at room temperature. To the mixture was added aqueous solution hydrochloric acid until pH 8, and washed with ethyl acetate. The water layer was neutralized by adding aqueous solution hydrochloric acid, and extracted with ethyl acetate. The extract was washed with a saturated aqueous solution of sodium chloride, dried over anhydrous magnesium sulfate and concentrated. The residue was recrystallized from the mixture solution of hexane/ethyl acetate (3:1) to give the title compound (9.83 g) having the following physical data.

TLC : Rf 0.30 (hexane:ethyl acetate=1:1).

Example 1

4-(2S-t-butyloxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



To a solution of the compound prepared in reference example 4 (748 mg), the compound prepared in reference example 7 (537 mg) and dimethylaminopyridine (64 mg) in dichloromethane (20 ml) was added 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (482 mg) at room temperature. The reaction mixture was stirred for 2h at room temperature. To the reaction mixture was added ethyl acetate, and washed with 1N aqueous solution hydrochloric acid (x2). The organic layer was dried over anhydrous magnesium sulfate and concentrated. The residue was purified by column chromatography on silica gel (hexane : ethyl acetate = 5 : 1) to give the title compound (1.04 g) having the following physical data.

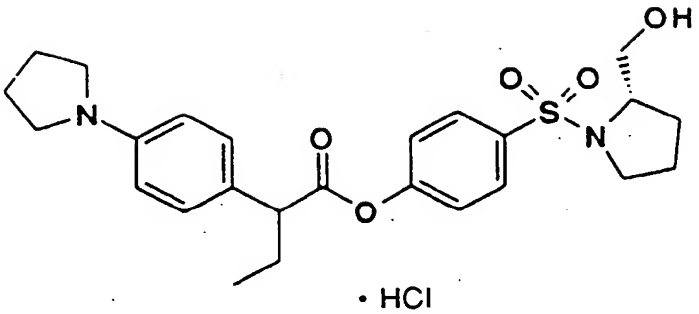
TLC : Rf 0.23 (hexane:ethyl acetate=5:1).

Example 1(1)~1(147)

By the same procedure as example 1 and by known method converted to corresponding salts or acid addition salts, the compounds having the following physical data were given by using corresponding phenol derivatives instead of the compound prepared in reference example 4 and by using corresponding carboxylic acid derivatives instead of the compound prepared in reference example 7.

Example 1(1)

4-(2S-hydroxymethylpyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

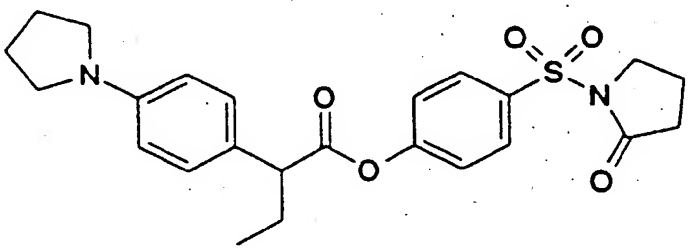


• HCl

NMR (DMSO-d_6): δ7.85 (2H, d, J=9Hz), 7.28 (2H, d, J=9Hz), 7.28 (2H, d, J=9Hz), 6.83 (2H, d, J=9Hz), 3.75 (1H, t, J=7Hz), 3.60-3.44 (2H, m), 3.40-3.20 (6H, m), 3.11-2.95 (1H, m), 2.21-1.90 (5H, m), 1.90-1.65 (3H, m), 1.55-1.30 (2H, m), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.48 (ethyl acetate:hexane=1:1).

Example 1(2)

4-(2-oxopyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl) butanoic acid ester · hydrochloride

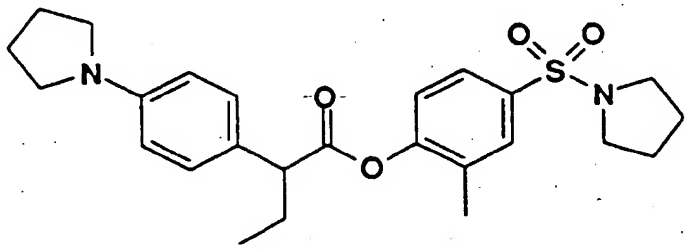


• HCl

NMR($CDCl_3$): δ8.05 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.6Hz), 7.47 (2H, d, J=8.6Hz), 7.19 (2H, d, J=8.8Hz), 3.89 (2H, t, J=7.2Hz), 3.74 (1H, t, J=7.8Hz), 3.85-3.45 (4H, brs), 2.44 (2H, t, J=7.8Hz), 2.40-2.25 (4H, m), 2.35-1.75 (2H, m), 2.20-2.00 (2H, m), 0.99 (3H, t, J=7.4Hz);
TLC : Rf 0.39 (ethyl acetate:hexane=1:1).

Example 1(3)

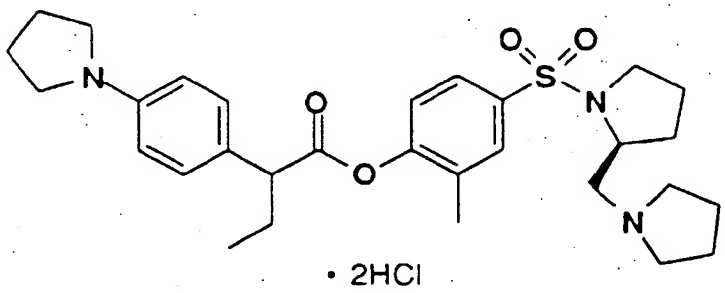
4-(pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.68-7.57 (2H, m), 7.23 (2H, d, J=8Hz), 7.06 (1H, d, J=8Hz), 6.55 (2H, d, J=8Hz), 3.61 (1H, t, J=7Hz), 3.35-3.13 (8H, m), 2.30-1.65 (13H, m), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.49 (ethyl acetate:hexane=3:7).

Example 1(4)

4-(2S-(pyrrolidin-1-ylmethyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

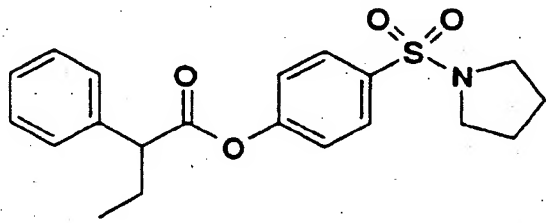


· 2HCl

NMR (CD_3OD): δ7.95-7.75 (2H, m), 7.65 (4H, s), 7.22 (1H, d, J=8.5Hz), 4.26-3.90 (2H, m), 3.99 (1H, t, J=7.5Hz), 3.90-3.70 (5H, m), 3.50-3.10 (6H, m), 2.40-2.25 (4H, m), 2.40-1.35 (10H, m), 2.07 (3H, s), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.43 (water:methanol:chloroform=1:10:90).

Example 1(5)

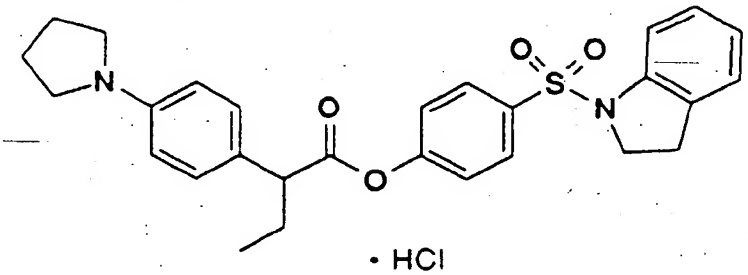
4-(pyrrolidin-1-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ7.85-7.74 (2H, m), 7.41-7.24 (5H, m), 7.23-7.10 (2H, m), 3.71 (1H, t, J=7Hz), 3.30-3.15 (4H, m), 2.39-2.10 (1H, m), 2.03-1.80 (1H, m), 1.80-1.68 (4H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.43 (hexane:ethyl acetate=2:1).

Example 1(6)

4-(indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

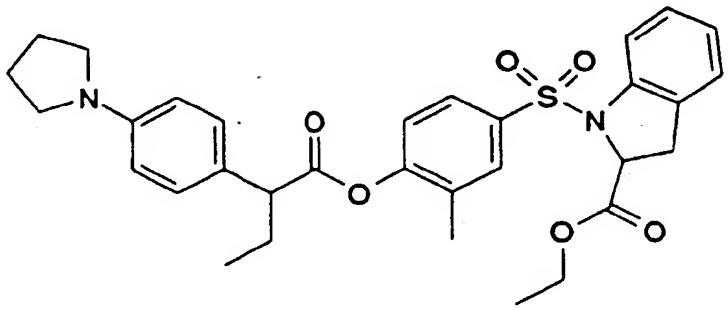


· HCl

NMR ($CDCl_3$): δ7.78 (2H, d, J=8.8Hz), 7.62 (1H, d, J=8.0Hz), 7.50-7.34 (4H, m), 7.24-7.12 (1H, m), 7.08 (3H, d, J=8.8Hz), 6.97 (1H, dt, J=1.0 and 7.2Hz), 3.90 (2H, d, J=8.4Hz), 3.68 (1H, t, J=7.6Hz), 3.70-3.45 (4H, m), 2.89 (2H, t, J=8.4Hz), 2.40-2.20 (4H, m), 2.30-2.05 and 2.00-1.75 (each 1H, m), 0.96 (3H, t, J=7.2Hz);
TLC : Rf 0.47 (ethyl acetate:hexane=1:2).

Example 1(7)

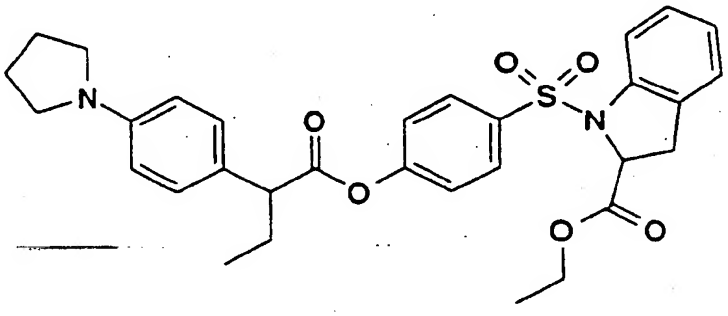
4-(2-(ethoxycarbonyl)indolin-1-ylsulfonyl)2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.7-7.5 (m, 3H), 7.2-6.9 (m, 6H), 6.8-6.4 (m, 2H), 4.71 (q. J=5.2Hz, 1H), 4.23 (q, J=7.2Hz, 2H), 3.57 (t, J=7.6Hz, 1H), 3.4-3.0 (m, 6H), 2.4-1.8 (m, 9H), 1.29 (t, J=7.2Hz, 3H), 1.0-0.9 (m, 3H);
TLC : Rf 0.63 (hexane:ethyl acetate=2:1).

Example 1(8)

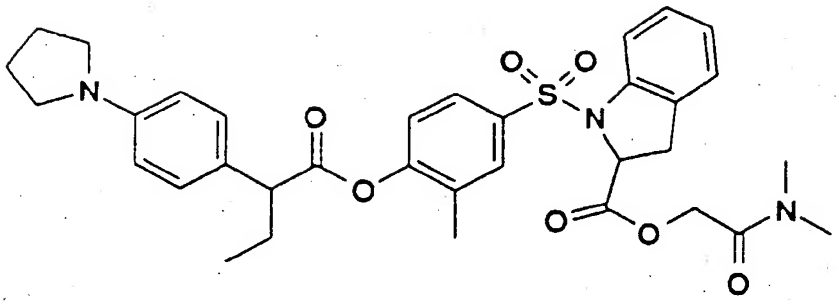
4-(2-(ethoxycarbonyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.77 (2H, d, J=8.5Hz), 7.53 (1H, d, J=8.0Hz), 7.24-6.93 (7H, m), 6.52 (2H, d, J=8.5Hz), 4.71 (1H, dd, J=10.0, 5.5Hz), 4.24 (2H, q, J=7.0Hz), 3.54 (1H, t, J=8.0Hz), 3.32-3.22 (4H, m), 3.22 (1H, dd, J=10.0, 16.0Hz), 3.06 (1H, dd, J=16.0, 5.5Hz), 2.05-1.90 (4H, m), 2.25-1.70 (2H, m), 1.29 (3H, t, J=7.0Hz), 0.95 (3H, t, J=7.5Hz);
TLC : Rf 0.57 (hexane:ethyl acetate=1:1).

Example 1(9)

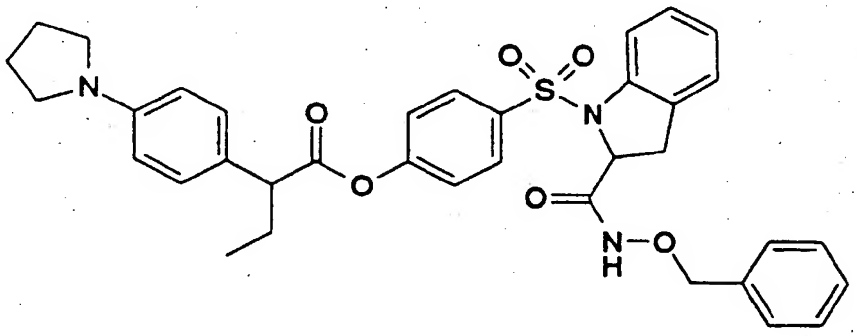
4-(2RS-(N,N-dimethylaminocarbonylmethoxycarbonyl)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.7-7.5 (m, 3H), 7.2-6.9 (m, 6H), 6.54 (d, J=8.6Hz, 2H), 4.85 (d. J=14.5Hz, 1H), 4.82 (dd, J=1.0, 10.8Hz, 1H), 4.70 (d, J=14.5Hz, 1H), 3.58 (t, J=7.7Hz, 1H), 3.65-3.50 (m, 1H), 3.45 (dd, J=10.8, 16.1Hz, 1H), 3.4-3.2 (m, 4H), 2.96 (s, 3H), 2.94 (s, 3H), 2.3-1.8 (m, 6H), 1.97 (s, 3H), 0.96 (t, J=7.4Hz, 3H);
TLC : Rf 0.52 (chloroform:ethyl acetate=1:1).

Example 1(10)

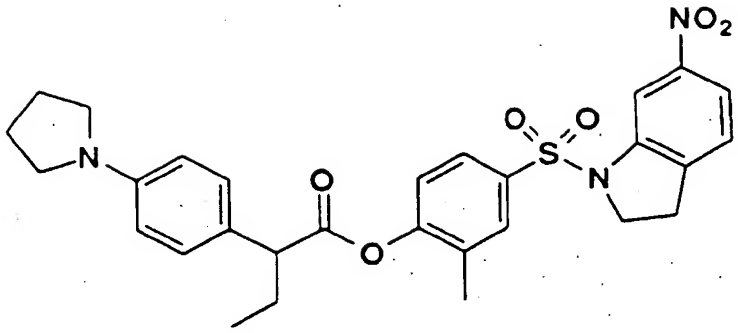
4-(2RS-(N-benzyloxycarbamoyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 9.22 (1H, s), 7.60 (1H, d, J=8.0Hz), 7.51 (2H, d, J=9.0Hz), 7.29 (5H, s), 7.17-7.00 (8H, m), 6.52 (2H, d, J=9.0Hz), 4.88 (2H, s), 4.60 (1H, dd, J=10.0Hz, 1.5Hz), 3.53 (1H, t, J=7.0Hz), 3.26 (5H, t-like, J=6.0Hz), 2.74 (1H, dd, J=16.0Hz, 10.0Hz), 2.20-1.77 (2H, m), 2.03-1.98 (4H, m), 0.92 (3H, t, J=7.0Hz);
TLC : Rf 0.44 (hexane:ethyl acetate=1:1).

Example 1(11)

4-(6-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

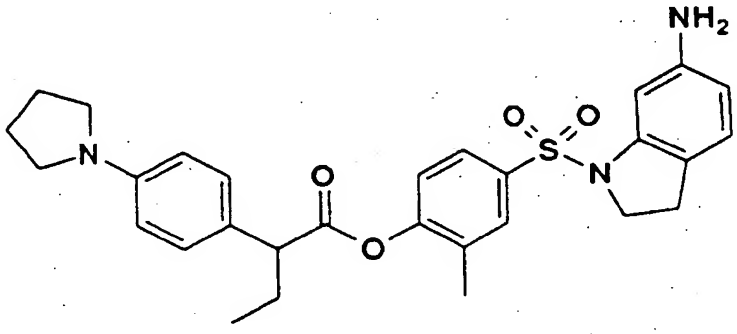


NMR ($CDCl_3$): δ 8.10 (dd, J=2.4, 8.8Hz, 1H), 7.96 (s, 1H), 7.7-7.6 (m, 3H), 7.18 (d, J=8.4Hz, 2H), 7.05 (d, J=8.0Hz, 1H) 6 52 (d, J=8.4Hz, 2H), 4.01 (t, J=8.6Hz, 2H), 3.58 (t, J=7.8Hz, 1H), 3.3-3.2 (m, 4H), 3.08 (t, J=8.6Hz, 2H), 2.3-1.8 (m 2H). 2.00 (s, 3H),2.1-19 (m, 4H), 0.96 (t, J=7.4Hz, 3H);

TLC : Rf 0.33 (hexane:ethyl acetate=3:1).

Example 1(12)

4-(6-aminoindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

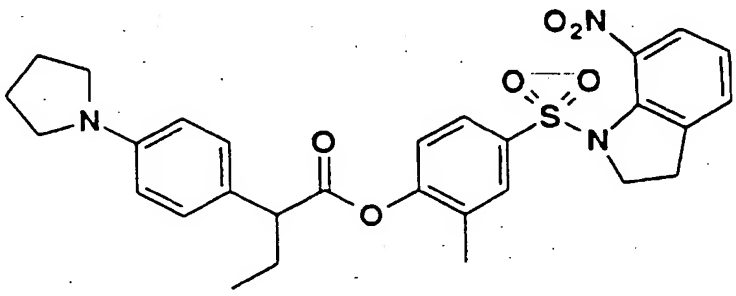


NMR ($CDCl_3$): δ 7.6-7.4 (m, 3H), 7.20 (d, J=8.7Hz, 2H), 6.94 (d, J=8.4Hz, 1H), 6.53 (d, J=8.7Hz, 2H), 6.6-6.4 (m, 2H), 3.83 (t, J=8.2Hz, 2H). 3.58 (t, J=7.7Hz, 1H), 3.4-3.2 (m, 4H), 2.64 (t, J=8.2Hz, 2H), 2.3-1.8 (m, 6H), 1.95 (s, 3H), 0.97 (t, J=7.4Hz, 3H);

TLC : Rf 0.59 (hexane:ethyl acetate=1:1).

Example 1(13)

4-(7-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

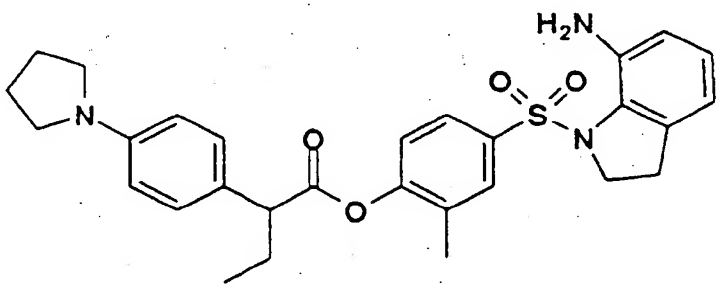


NMR ($CDCl_3$): δ 8.38 (d, J=2.2Hz, 1H), 7.85 (dd, J=2.0, 8.4Hz, 1H), 7.8-7.6 (m, 2H), 7.2-7.1 (m, 1H), 7.18 (d, J=8.6Hz,2H), 7.03 (d, J=8.2Hz, 1H), 6.52 (d, J=8.6Hz, 2H), 3.99 (t, J=8.6Hz, 2H), 3.58 (t, J=7.6Hz, 1H), 3.3-3.2 (m, 4H), 3.05 (t, J=8.6Hz, 2H), 2.3-1.7 (m, 9H), 0.96 (t, J=7.4Hz, 3H);

TLC : Rf 0.49 (hexane:ethyl acetate=1:1).

Example 1(14)

4-(7-aminoindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

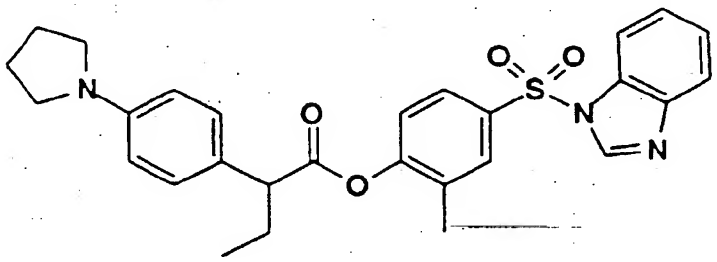


NMR ($CDCl_3$): δ 7.6-7.5 (m, 2H), 7.15 (d, J=8.6Hz, 2H), 7.0-6.9 (m, 2H), 6.82 (d, J=8.0Hz, 1H), 6.52 (d, J=8.6Hz, 2H), 6.29 (dd, J=2.0, 8.0Hz, 1H), 3.84 (t, J=8.0Hz, 2H), 3.58 (t, J=7.6Hz, 1H), 3.4-3.2 (m, 4H), 2.76 (t, J=7.6Hz, 2H), 2.3-1.8 (m, 9H), 0.97 (t, J=7.4Hz, 3H);

TLC : Rf 0.40 (hexane:ethyl acetate=2:1).

Example 1(15)

4-(benzimidazol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

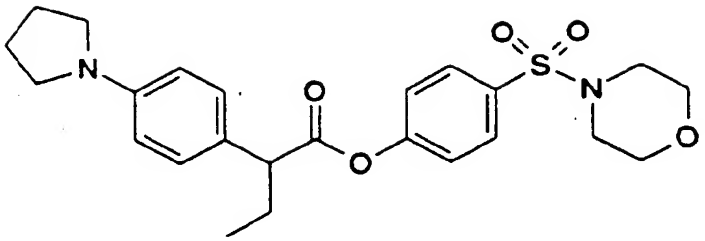


NMR ($CDCl_3$): δ 8.35 (1H, s), 7.79 (4H, m), 7.35 (2H, m), 7.17 (2H, d, J=8.8Hz), 7.08 (1H, d, J=9.4Hz), 6.52 (2H, d, J=8.8Hz), 3.57 (1H, t, J=7.8Hz), 3.26 (4H, m), 2.10 (1H, m), 2.00 (3H, s), 1.97 (4H, m), 1.88 (1H, m), 0.95 (3H, t, J=7.4Hz);

TLC : Rf 0.49 (hexane:ethyl acetate=2:1).

Example 1(16)

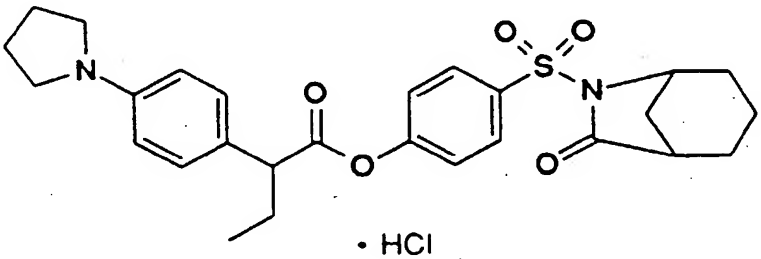
4-(morpholin-4-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 7.75 (2H, d, J=7Hz), 7.27 (2H, d, J=7Hz), 7.16 (2H, d, J=7Hz), 6.52 (2H, d, J=7Hz), 3.67 (1H, t, J=7Hz), 3.61 (4H, t-like), 3.20 (4H, t-like), 2.83 (4H, t-like), 2.04 (1H, m), 1.94 (4H, t-like), 1.79 (1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.54 (hexane:ethyl acetate=1:1).

Example 1(17)

4-(6-aza-7-oxo-bicyclo[3.2.1]octan-6-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

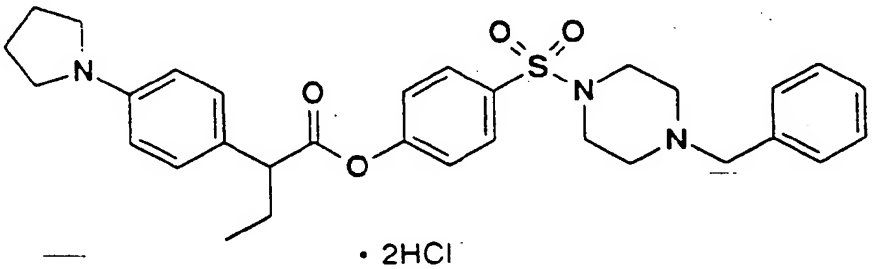


• HCl

NMR ($CDCl_3$): δ 8.19 (2H, d, J=9Hz), 7.38 (2H, d, J=9Hz), 7.19 (4H, d, J=9Hz), 4.65-4.55 (1H, m), 3.68 (1H, t, J=7Hz), 3.61-3.37 (4H, m), 2.59-2.49 (1H, m), 2.35-1.46 (12H, m), 1.35-1.10 (2H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.17 (ethyl acetate:hexane=1:3).

Example 1(18)

4-(4-benzylpiperazin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

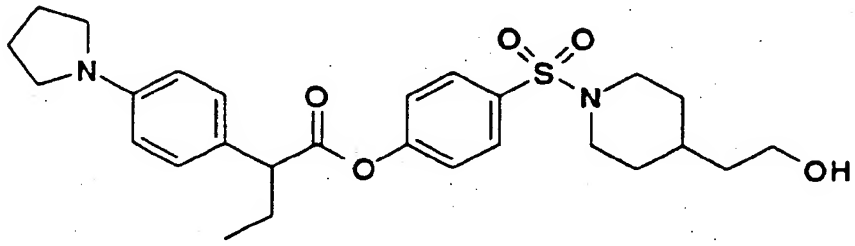


• 2HCl

NMR (CD_3OD): δ 7.83 (2H, d, J=8.6Hz), 7.75-7.40 (9H, m), 7.29 (2H, d, J=8.6Hz), 4.35 (2H, s), 4.00-3.62 (7H, m), 3.60-3.40 (2H, m), 3.30-3.10 (2H, m), 2.98-2.72 (2H, m), 2.38-2.10 (5H, m), 2.04-1.80 (1H, m), 0.99 (3H, t, J=7.4Hz);
TLC:Rf 0.40 (ethyl acetate:hexane=3:7).

Example 1(19)

4-(4-(2-hydroxyethyl)piperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

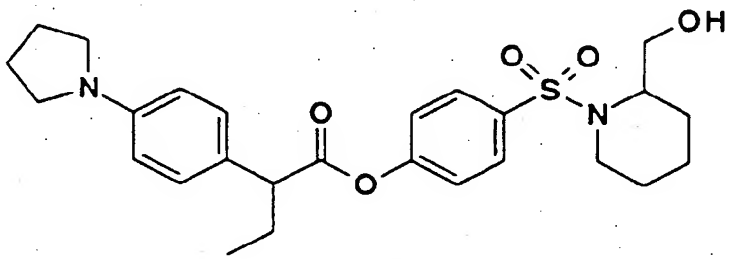


NMR ($CDCl_3$): δ 7.71 (2H, d, J=9.0Hz), 7.72 (2H, d, J=8.7Hz), 7.15 (2H, d, J=9.0Hz), 6.55 (2H, d, J=8.7Hz), 3.74 (2H, d, J=10.2Hz), 3.63 (2H, t, J=6.0Hz), 3.58 (1H, t, J=8.0Hz), 3.36-3.22 (4H, m), 2.35-1.78 (8H, m), 1.72 (2H, d, J=10.0Hz), 1.54-1.20 (5H, m), 0.98 (3H, t, J=7.4Hz);

TLC : Rf 0.52 (chloroform:methanol=19:1).

Example 1(20)

4-(2RS-hydroxymethylpiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



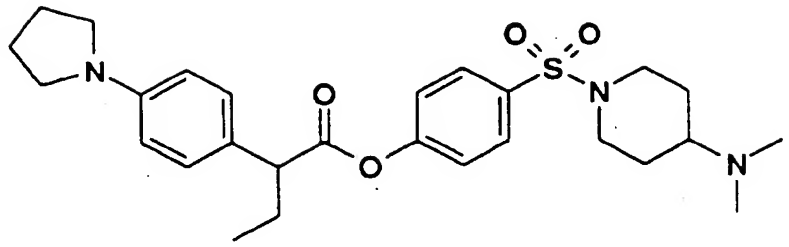
• HCl

NMR (DMSO-d_6): δ 7.85 (2H, d, J=9Hz), 7.27 (2H, d, J=9Hz), 7.22 (2H, d, J=9Hz), 6.83 (2H, d, J=9Hz), 3.93-3.80 (1H, m), 3.75 (1H, t, J=7Hz), 3.69-3.45 (2H, m), 3.45-3.20 (5H, m), 3.06-2.88 (1H, m), 2.21-1.80 (5H, m), 1.80-1.64 (2H, m), 1.55-1.30 (3H, m), 1.30-0.99 (2H, m), 0.90 (3H, t, J=7Hz);

TLC : Rf 0.46 (ethyl acetate:hexane=1:1).

Example 1(21)

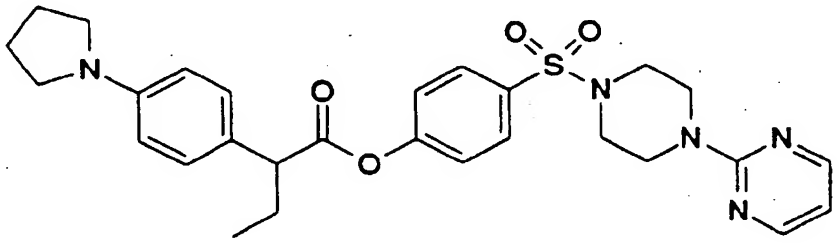
4-(4-(N,N-dimethylamino)piperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.71 (2H, d, J=8.7Hz), 7.20 (2H, d, J=8.8Hz), 7.16 (2H, d, J=8.7Hz), 6.54 (2H, d, J=8.8Hz), 3.75 (2H, d, J=13.7Hz), 3.58 (1H, t, J=7.7Hz), 3.29 (4H, t, J=6.6Hz), 2.36-1.53 (19H, m), 0.98 (3H, t, J=7.4Hz);
TLC : Rf 0.25 (hexane:ethyl acetate=2:1).

Example 1(22)

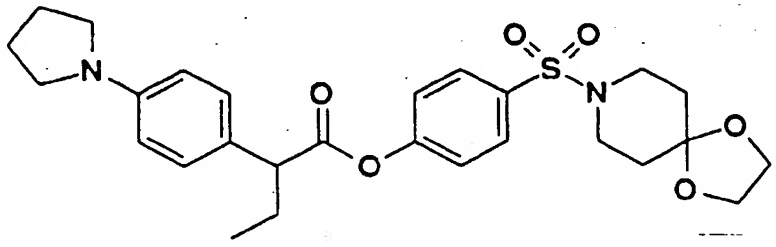
4-(4-(pyrimidin-2-yl)piperazin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 8.26 (2H, d, J=8.8Hz), 7.72 (2H, d, J=8.7Hz), 7.22-7.12 (4H, m), 6.56-6.47 (3H, m), 3.93 (4H, t, J=5.2Hz), 3.57 (1H, t, J=7.7Hz), 3.31-3.25 (4H, m), 3.04 (4H, t, J=5.1Hz), 2.25-1.65 (6H, m), 0.97 (3H, t, J=7.3Hz);
TLC : Rf 0.43 (hexane:ethyl acetate=1:1).

Example 1(23)

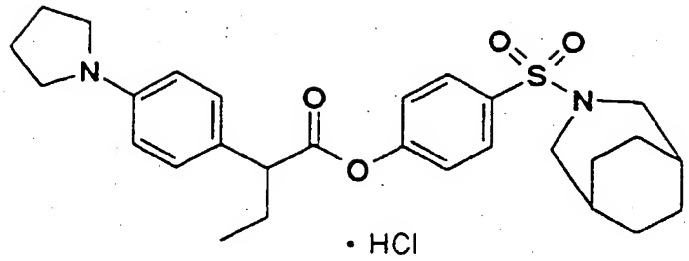
4-(1,4-dioxa-8-azaspiro[4.5]decan-8-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.72 (2H, d, J=8.7Hz), 7.24-7.15 (4H, m), 6.56 (2H, d, J=8.7Hz), 3.89 (4H, s), 3.59 (1H, t, J=7.7Hz), 3.29 (4H, t, J=6.6Hz), 3.14 (4H, t, J=5.7Hz), 2.30-1.61 (10H, m), 0.98 (3H, t, J=7.4Hz);
TLC : Rf 0.48 (hexane:ethyl acetate=1:1).

Example 1(24)

4-(3-azabicyclo[3.2.2]nonan-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



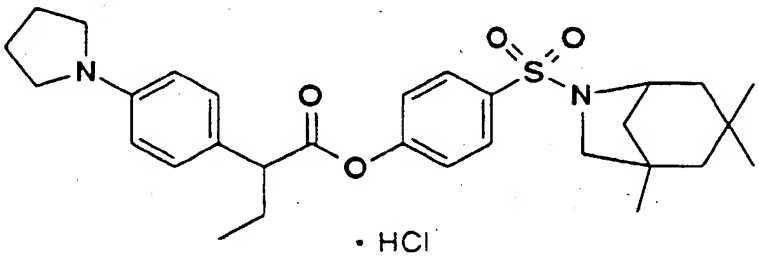
• HCl

NMR ($CDCl_3$): δ 7.73 (2H, d, J=8.6Hz), 7.53 (2H, d, J=8.6Hz), 7.45 (2H, d, J=8.6Hz), 7.15 (2H, d, J=8.8Hz), 3.72 (1H, t, J=7.6Hz), 3.75-3.50 (4H, m), 3.22 (4H, d, J=4.2Hz), 2.40-2.20 (4H, m), 2.40-1.75 (2H, m), 2.10-2.00 (2H, m), 1.80-1.50 (8H, m), 0.99 (3H, t, J=7.4Hz);

TLC : Rf 0.57 (ethyl acetate:hexane=1:3).

Example 1(25)

4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]octan-6-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



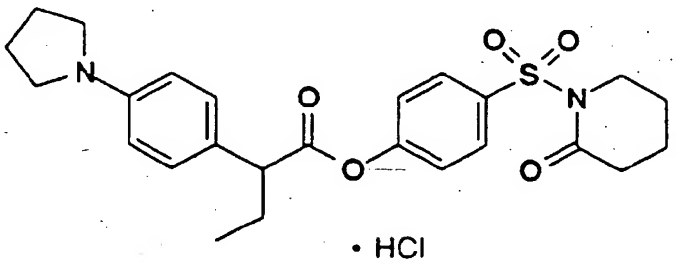
• HCl

NMR ($CDCl_3$): δ 7.81 (2H, d, J=8.8Hz), 7.40 (2H, d, J=8.4Hz), 7.36-7.18 (2H, brs), 7.15 (2H, d, J=8.8Hz), 4.08 (1H, t-like), 3.69 (1H, t, J=7.8Hz), 3.64-3.38 (4H, ml, 3.32 (1H, d, J=9.6Hz), 2.76 (1H, dd, J=9.6 and 1.4Hz), 2.36-2.08 (5H, m), 2.02-1.76 (2H, m), 1.52 (2H, d, J=14.4Hz), 1.34 (2H, d, J=12.4Hz), 1.22 (3H, s), 1.16-1.02 (1H, m), 0.99 (3H, t, J=7.4Hz), 0.94 (3H, s), 0.92 (3H, s);

TLC : Rf 0.54 (ethyl acetate:hexane=1:3).

Example 1(26)

4-(2-oxopiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



• HCl

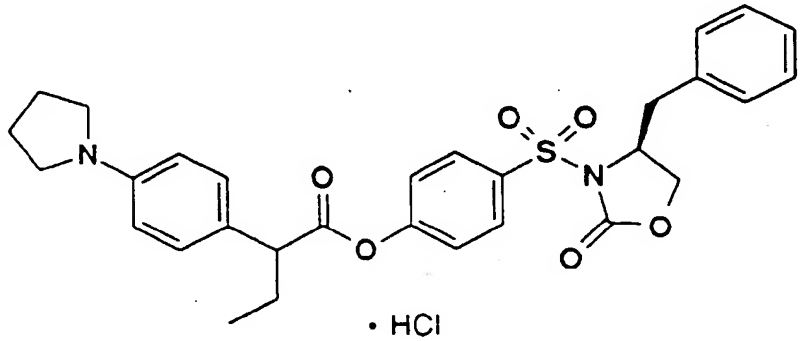
NMR ($CDCl_3$): δ 8.03 (2H, d, J=9.0Hz), 7.65 (2H, d, J=8.6Hz), 7.48 (2H, d, J=8.6Hz), 7.17 (2H, d, J=9.0Hz), 3.89

(2H, t, J=5.8Hz),3.74 (1H, t, J=7.8Hz), 3.80-3.50 (4H, m), 2.42 (2H, t, J=6.6Hz), 2.50-2.25 (4H, m), 2.40-1.70 (2H, m), 2.00-1.70 (4H, m), 0.99 (3H, t, J=7.4Hz);

TLC : Rf 0.83 (acetic acid:methanol:chloroform=1:2:40).

Example 1(27)

4-(2-oxo-4S-benzyltetrahydroxazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



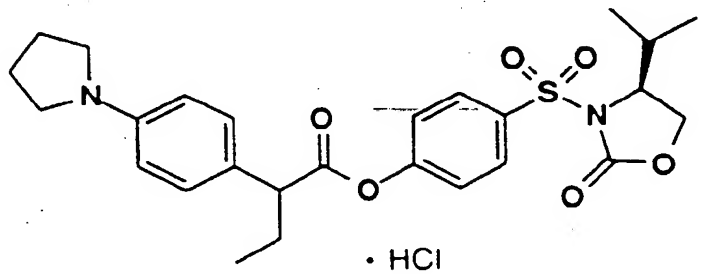
· HCl

NMR ($CDCl_3$): δ 8.13 (2H, d, J=8.8Hz), 7.64 (2H, d, J=8.8Hz), 7.48 (2H, d, J=8.8Hz), 7.23 (2H, d, J=8.8Hz), 7.40-7.16 (5H, m), 4.75-4.58 (1H, m), 4.24-4.05 (2H, m), 3.76 (1H, t, J=7.6Hz), 3.85-3.50 (4H, brs), 3.50 (1H, dd, J=13.2, 3.8Hz), 2.83 (1H, dd, J=13.2, 10.2Hz), 2.44-2.26 (4H, m), 2.34-2.10 and 2.10-1.76 (each 1H, m), 0.99 (3H, t, J=7.4Hz);

TLC : Rf 0.51 (ethyl acetate:hexane=1:2).

Example 1(28)

4-(2-oxo-4S-isopropylperhydroxazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



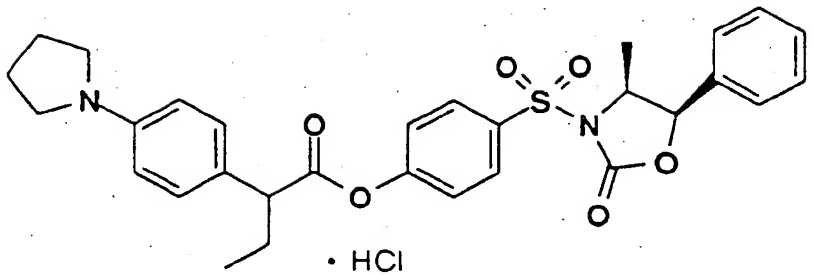
· HCl

NMR($CDCl_3$): δ 8.10 (2H, d, J=9.0Hz), 7.63 (2H, d, J=8.6Hz), 7.48 (2H, d, J=8.6Hz), 7.22 (2H, d, J=9.0Hz), 4.43 (1H, dt, J=8.2, 3.0Hz), 4.29 (1H, t, J=8.8Hz), 4.16 (1H, dd, J=8.8, 3.0Hz), 3.75 (1H, t, J=7.6Hz), 3.90-3.45 (4H, brs), 2.56-1.76 (7H, m), 0.99 (3H, t, J=7.2Hz), 0.93 (3H, d, J=6.8Hz), 0.75 (3H, d, J=6.8Hz);

TLC : Rf 0.62 (ethyl acetate:hexane=1:1).

Example 1(29)

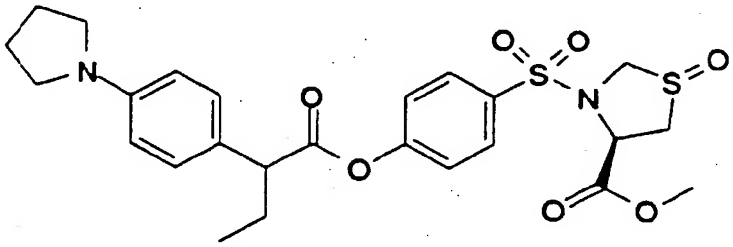
4-(2-oxo-4S-methyl-5S-phenylperhydroxazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ 8.13 (2H, d, J=8.8Hz), 7.72 (2H, d, J=8.8Hz), 7.51 (2H, d, J=8.8Hz), 7.46-7.34 (3H, m), 7.23 (2H, d, J=8.8Hz), 7.30-7.20 (2H, m), 5.71 (1H, d, J=7.2Hz), 4.78 (1H, dq, J=7.2Hz), 3.77 (1H, t, J=7.2Hz), 3.90-3.50 (4H, brs), 2.50-2.25 (4H, brs), 2.40-1.80 (2H, m), 1.00 (3H, t, J=7.2Hz), 0.97 (3H, d, J=7.2Hz);
TLC : Rf 0.66 (ethyl acetate:hexane=1:2).

Example 1(30)

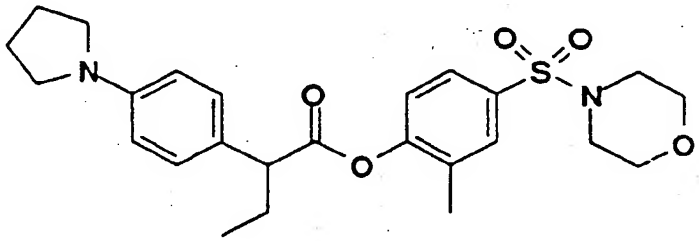
4-(1RS-oxo-4S-methoxycarbonylperhydrothiazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.87 (2H, d, J=9.0Hz), 7.21 (2H, d, J=9.0Hz), 7.19 (2H, d, J=9.0Hz), 6.55 (2H, d, J=9.0Hz), 5.28-5.16 (2H, ml, 4.09-4.01 (1H, m), 3.69-3.44 (5H, m), 3.33-3.26 (4H, m), 3.08-2.97 (1H, m), 2.24-1.80 (6H, m), 0.98 (3H, t, J=7.4Hz);
TLC : Rf 0.50 (chloroform:methanol:acetic acid=40:2:1).

Example 1(31)

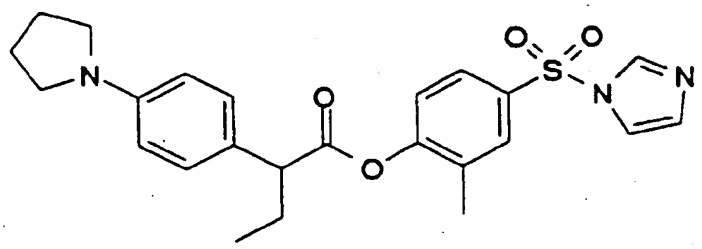
4-(morpholin-4-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.56-7.51 (2H, m), 7.26-7.21 (2H, m), 7.10 (1H, d, J=8Hz), 6.55 (2H, d, J=8Hz), 3.75-3.71 (4H, m), 3.62 (1H, t, J=8Hz), 3.32-3.26 (4H, m), 3.01-2.96 (4H, m), 2.37-1.73 (2H, m), 2.06 (3H, s), 2.04-1.96 (4H, m), 1.00 (3H, t, J=8Hz);
TLC : Rf 0.27 (hexane:ethyl acetate=3:1).

Example 1(32)

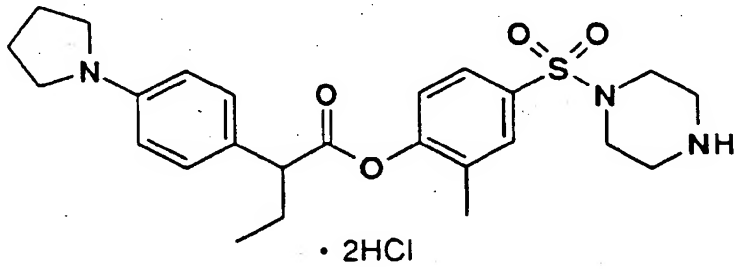
4-(imidazol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.99 (1H, m), 7.75 (1H, s), 7.72 (1H, m), 7.27-7.08 (5H, m), 6.54 (2H, d, J=8.8Hz), 3.60 (1 H, t, J=7.6Hz), 3.28 (4H, m), 2.14 (1 H,m), 2.04 (3H, s), 2.01 (4H, m), 1.91 (1H, m), 0.97 (3H, t, J=7.4Hz);
TLC : Rf 0.36 (hexane:ethyl acetate=2:1).

Example 1(33)

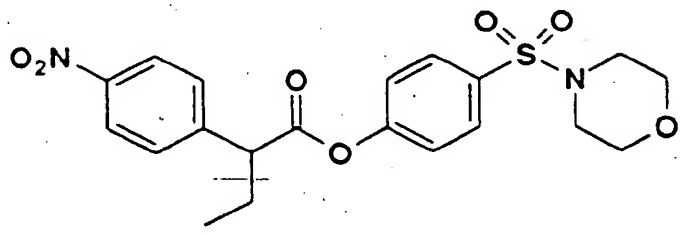
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (CD_3OD): δ 7.80-7.56 (6H, m), 7.18 (1H, d, J=8.2Hz), 4.00 (1H, t, J=7.6Hz), 3.90-3.72 (4H, m), 3.30 (8H, s-like), 2.43-2.15 (5H, m), 2.06 (3H, s), 2.15-1.84 (1H, m), 1.00 (3H, t, J=7.2Hz);
TLC : Rf 0.53 (chloroform:methanol:acetic acid=15:2:1).

Example 1(34)

4-(morpholin-4-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester

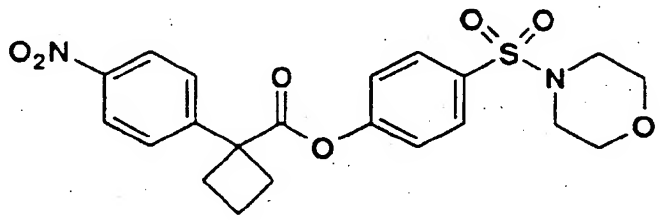


NMR ($CDCl_3$): δ 8.26 (2H, d, J=8Hz), 7.77 (2H, d, J=8Hz), 7.59 (2H, d, J=8Hz), 7.20 (2H, d, J=8Hz), 3.86 (1H, t, J=7Hz), 3.80-3.68 (4H, m), 3.06-2.94 (4H, m), 2.30 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.97 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.03 (3H, t, J=7Hz);

TLC : Rf 0.16 (hexane:ethyl acetate=7:3).

Example 1(35)

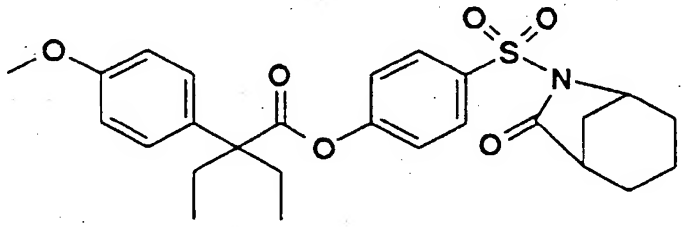
4-(morpholin-4-ylsulfonyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR ($CDCl_3$): δ 8.26 (2H, d, J=8Hz), 7.77 (2H, d, J=8Hz), 7.56 (2H, d, J=8Hz), 7.16 (2H, d, J=8Hz), 3.79-3.66 (4H, m), 3.15-2.91 (6H, m), 2.80-2.60 (2H, m), 2.39-1.91 (2H, m);
TLC : Rf 0.16 (hexane:ethyl acetate=7:3).

Example 1(36)

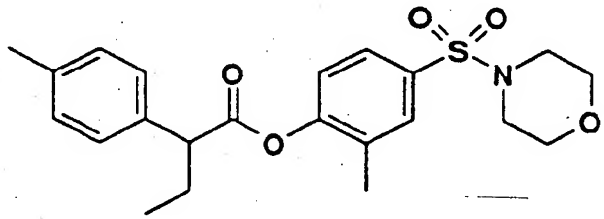
4-(6-aza-7-oxobicyclo[3.2.1]octan-6-ylsulfonyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester



NMR ($CDCl_3$): δ 8.08 (2H, d, J=8.8Hz), 7.27 (2H, d, J=8.8Hz), 7.11 (2H, d, J=8.8Hz), 6.91 (2H, d, J=8.8Hz), 4.59 (1H, brt, J=4.8Hz), 3.82 (3H, s), 2.53 (1H, brs), 2.32-1.15 (12H, m), 0.84 (6H, t, J=7.4Hz);
TLC : Rf 0.85 (acetic acid:methanol:chloroform=1:2:40).

Example 1(37)

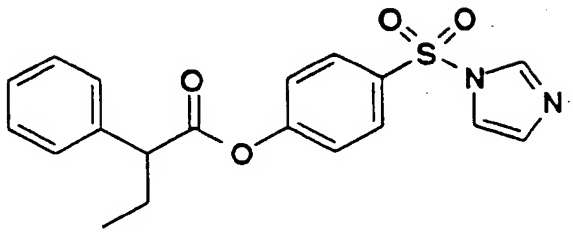
4-(morpholin-4-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.57-7.52 (2H, m), 7.30-7.08 (5H, m), 3.75-3.67 (5H, m), 3.01-2.96 (4H, m), 2.36 (3H, s), 2.32-2.13 and 2.03-1.82 (eachI H, m), 2.02 (3H, s), 1.00 (3H, t, J=7Hz);
TLC : Rf 0.30 (hexane:ethyl acetate=3:1).

Example 1(38)

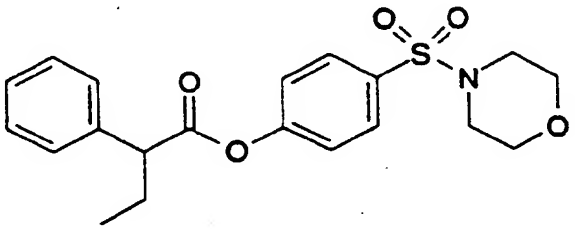
4-(imidazol-1-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.99 (1H, s), 7.97-7.86 (2H, m), 7.40-7.28 (5H, m), 7.28-7.25 (1H, m), 7.25-7.15 (2H, m), 7.13-7.05 (1H, m), 3.68 (1H, t, J=7Hz), 2.34-2.05 (1H, m), 2.05-1.98 (1H, m), 0.96 (3H, t, J=7Hz);
TLC : Rf 0.29 (hexane:ethyl acetate=6:4).

Example 1(39)

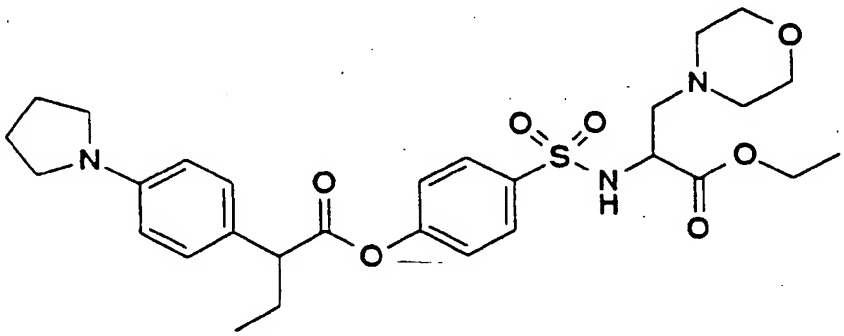
4-(morpholin-4-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.78-7.67 (2H, m), 7.43-7.24 (5H, m), 7.24-7.15 (2H, m), 3.78-3.65 (5H, m), 3.03-2.93 (4H, m), 2.36-2.11 (1H, m), 2.05-1.80 (1H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.26 (hexane:ethyl acetate=2:1).

Example 1(40)

4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

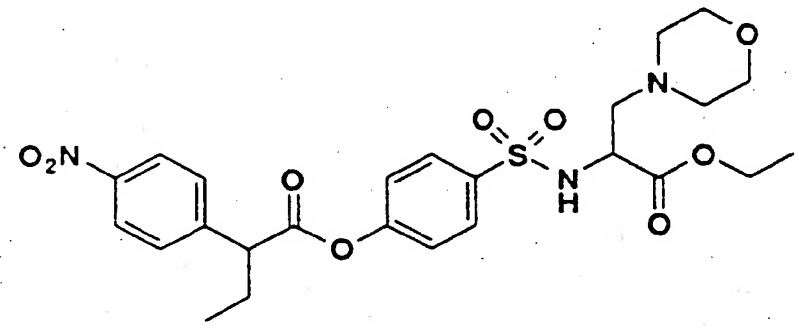


NMR ($CDCl_3$): δ 7.84 (2H, d, J=8.6Hz), 7.20 (2H, d, J=8.6Hz), 7.12 (2H, d, J=8.6Hz), 6.55 (2H, d, J=8.6Hz), 4.01 (3H, m), 3.57 (5H, m), 3.29 (4H, t, J=6.4Hz), 2.63 (2H, m), 2.36 (4H, m), 2.14 (1H, m), 2.01 (4H, m), 1.89 (1H, m), 1.17

(3H, t, J=7.0Hz), 0.97 (3H,t,J=7.4Hz);
TLC : Rf 0.34 (hexane:ethyl acetate=1:1).

Example 1(41)

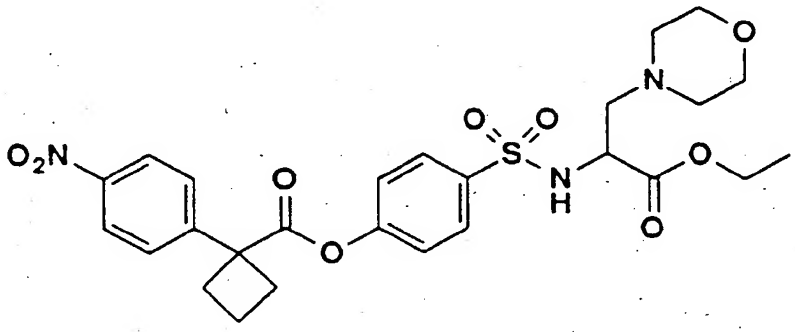
4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR ($CDCl_3$): δ 8.26 (2H, d, J=8.8Hz), 7.89 (2H, d, J=8.6Hz), 7.57 (2H, d, J=8.8Hz), 7.13 (2H, d, J=8.6Hz), 4.03 (2H, q, J=7.2Hz), 3.96 (1H, t, J=7.0Hz), 3.84 (1H, t, J=7.0Hz), 3.58 (4H, m), 2.68 (1H, dd, J=13.1, 7.0Hz), 2.61 (1H, dd, J=13.1, 7.0Hz), 2.36 (4H, m), 2.82 (1H, m), 1.95 (1H, dq, J=13.6, 7.2Hz), 1.17 (3H, t, J=7.2Hz), 1.02 (3H, t, J=7.2Hz);
TLC : Rf 0.45 (ethyl acetate).

Example 1(42)

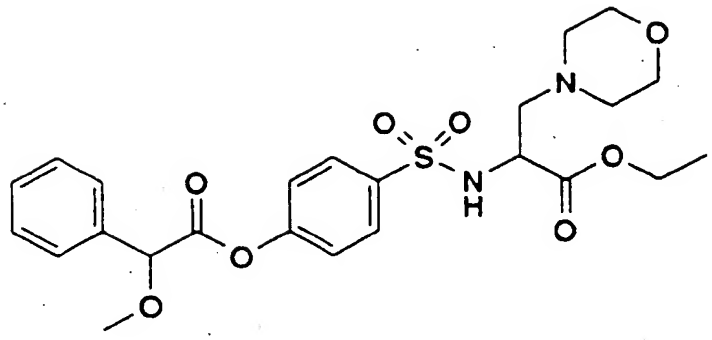
4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR ($CDCl_3$): δ 8.26 (2H, d, J=8.8Hz), 7.86 (2H, d, J=8.8Hz), 7.55 (2H, d, J=8.8Hz), 7.09 (2H, d, J=8.8Hz), 4.03 (2H, q, J=7.2Hz), 3.95 (1H, t, J=6.2Hz), 3.57 (4H, t, J=5.2Hz), 3.05 (2H, m), 2.67 (2H, m), 2.66 (1H, dd, J=12.6, 6.2Hz), 2.60 (1H, dd, J=12.6, 6.2Hz), 2.35 (4H, t, J=5.2Hz), 2.23 (1H, m), 2.04 (1H, m), 1.17 (3H, t, J=7.2Hz);
TLC : Rf 0.40 (chloroform:methanol:water=9:1:0.1).

Example 1(43)

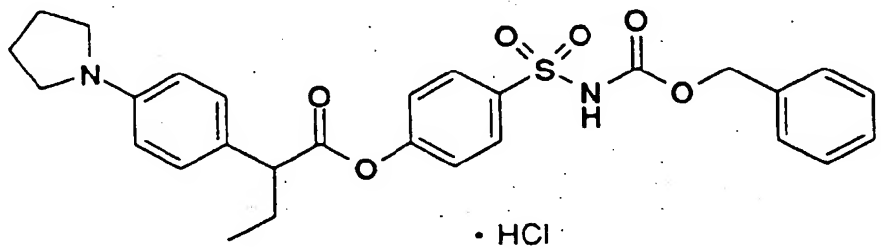
4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-phenyl-2-methoxyacetic acid ester



NMR ($CDCl_3$): δ 7.86 (2H, d, J=8.8Hz), 7.52 (2H, m), 7.42 (3H, m), 7.12 (2H, d, J=8.8Hz), 5.00 (1H, s), 4.01 (2H, q J=7.0Hz), 3.94 (1H, t, J=6.6Hz), 3.57 (4H, t, J=5.2Hz), 3.49 (3H, s), 2.66 (1H, dd, J=12.8, 6.6Hz), 2.60 (1H, dd, J 12 8. 6.6Hz), 2.34 (4H, t, J=5.2Hz), 1.16 (3H, t, J=7.0Hz);
TLC : Rf 0.26 (hexane:ethyl acetate=1:1).

Example 1(44)

4-(N-benzyloxycarbonylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

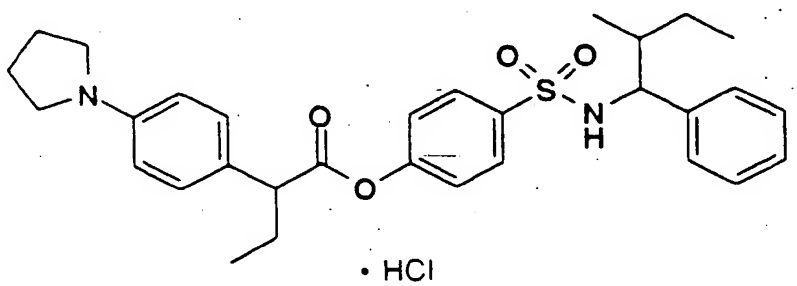


· HCl

NMR ($CDCl_3$): δ 8.3-8.0 (1H, brs), 8.00 (2H, d, J=8.8Hz), 7.56 (2H, d-like), 7.46 (2H, d-like), 7.38-7.22 (5H, m), 7.15 (2H, d, J=8.8Hz), 5.07 (2H, s), 3.74 (1H, t, J=7.8Hz), 3.8-3.5 (4H, m), 2.4-2.2 (4H, m), 2.40-2.10 and 2.10-1.80 (each 1H, m), 1.00 (3H, t, J=7.2Hz);
TLC : Rf 0.50 (acetic acid:ethyl acetate:hexane=1:8:16).

Example 1(45)

4-(N-1RS-phenyl-2RS-methylbutylsulfamoyl)phenyl 2BS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

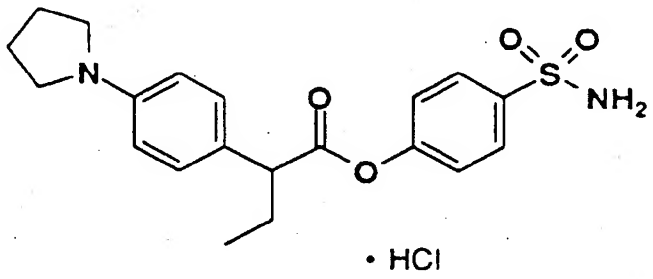


· HCl

NMR ($CDCl_3$): δ 7.80-7.57 (2H, m), 7.57-7.32 (4H, m), 7.12-6.93 (3H, m), 6.93-6.70 (4H, m), 5.38 (1H, m), 4.19-3.99 (1H, m), 3.90-3.30 (5H, m), 2.50-2.04 (5H, m), 1.96-1.40 (3H, m), 1.28-0.57 (10H, m);
TLC : Rf 0.24 (ethyl acetate:hexane=1:4).

Example 1(46)

4-sulfamoylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

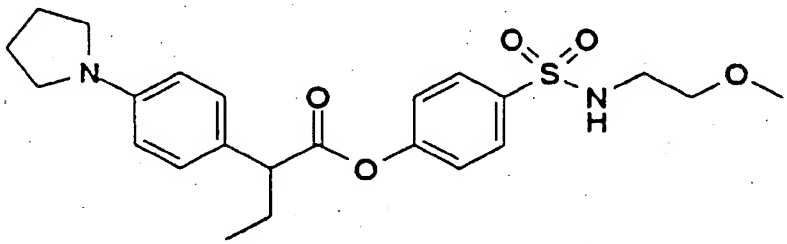


• HCl

NMR (CD_3OD): δ 7.88 (2H, d, J=8.6Hz), 7.18 (2H, d, J=8.8Hz), 7.11 (2H, d, J=8.8Hz), 6.57 (2H, d, J=8.6Hz), 3.61 (1H, t, J=7.6Hz), 3.34-3.19 (4H, m). 2.26-2.00 and 2.00-1.70 (each 1H, m), 2.07-1.96 (4H, m), 0.96 (3H, t, J=7.4Hz);
TLC : Rf 0.22 (acetic acid:methanol:chloroform=1:2:40).

Example 1(47)

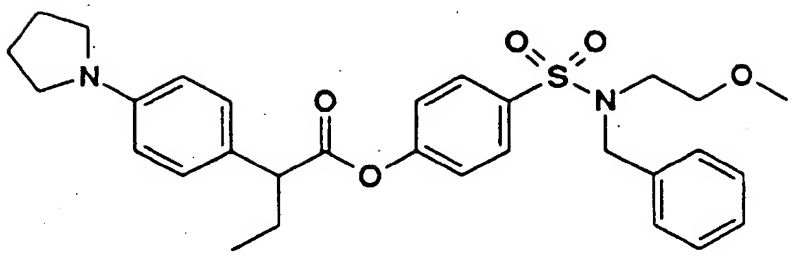
4-(N-2-methoxyethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.83 (2H, d, J=9.0Hz), 7.22 (2H, d, J=8.6Hz), 7.14 (2H, d, J=9.0Hz), 6.56 (2H, d, J=8.6Hz), 4.85 (1H, br), 3.59 (1H, t, J=7.7Hz), 3.42-3.20 (9H, m), 3.11 (2H, m), 2.28-1.70 (6H, m), 0.98 (3H, t, J=7.6Hz);
TLC : Rf 0.55 (hexane:ethyl acetate=2:3).

Example 1(48)

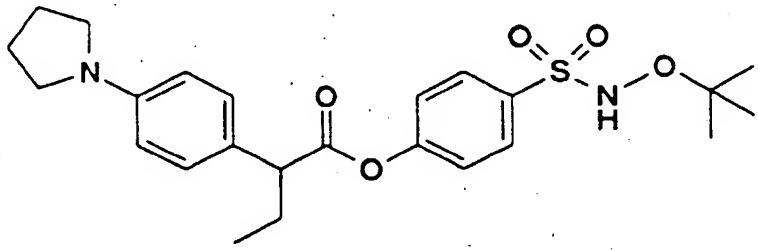
4-(N-2-methoxyethyl-N-benzylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.82 (2H, d, J=6.8Hz), 7.29 (5H, s), 7.19 (2H, d, J=8.6Hz), 7.13 (2H, d, J=6.8Hz), 6.56 (2H, d, J=8.6Hz), 4.40 (2H, s), 3.60(1H, t, J=7.4Hz), 3.2-3.4 (8H, m), 3.10 (3H, s), 1.8-2.3 (6H, m), 0.99 (3H, t, J=7.3Hz);
TLC : Rf 0.40 (hexane:ethyl acetate=3:1).

Example 1(49)

4-(N-t-butyloxysulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

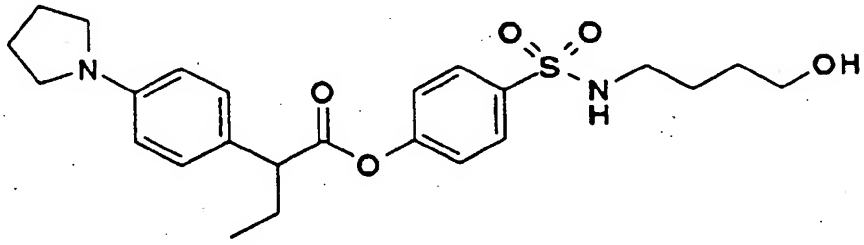


• HCl

NMR ($CDCl_3$): δ 7.88 (2H, d, J=8.8Hz), 7.24-7.15 (4H, m), 6.56 (2H, d, J=8.2Hz), 6.44 (1H, s), 3.59 (1H, t, J=7.2Hz), 3.33-3.26 (4H, m), 2.45-1.80 (6H, m), 1.21 (9H, s), 0.98 (3H, t, J=7.2Hz);
TLC : Rf 0.40 (hexane:ethyl acetate:acetic acid=5:2:0.1).

Example 1(50)

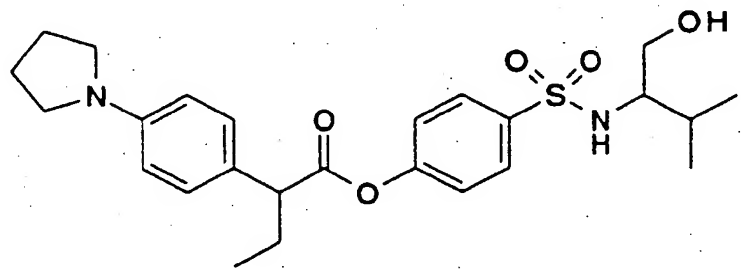
4-(N-4-hydroxybutylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.82 (2H, d, J=8.7Hz), 7.22 (2H, d, J=8.6Hz), 7.13 (2H, d, J=8.7Hz), 6.56 (2H, d, J=8.6Hz), 5.00 (1H, t, J=5.2Hz), 3.70-3.48 (3H, m), 3.40-3.12 (4H, m), 3.06-2.86 (2H, m), 2.30-1.76 (6H, m), 1.78-1.62 (1H, brs), 1.60-1.40 (4H, m), 0.97 (3H, t, J=7.4Hz);
TLC : Rf 0.48 (ethyl acetate).

Example 1(51)

4-(N-1RS-hydroxymethyl-2-methylpropylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

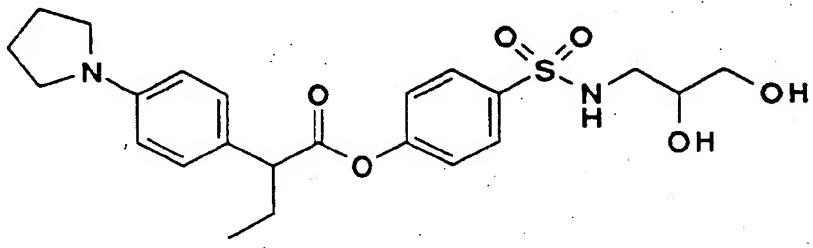


NMR ($CDCl_3$): δ 7.85 (2H, d, J=8.4Hz), 7.21 (2H, d, J=8.6Hz), 7.12 (2H, d, J=8.4Hz), 6.55 (2H, d, J=8.6Hz), 5.06 (1H, d, J=8.4Hz), 3.58 (1H, t, J=5.8Hz), 3.56-3.48 (2H, m), 3.36-3.22 (4H, m), 3.10-2.90 (1H, m), 2.23-1.65 (8H, m), 0.97 (3H, t, J=7.2Hz), 0.78 (6H, d, J=6.8Hz);

TLC : Rf 0.25 (ethyl acetate:hexane=2:3).

Example 1(52)

4-(N-2RS,3-dihydroxypropylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

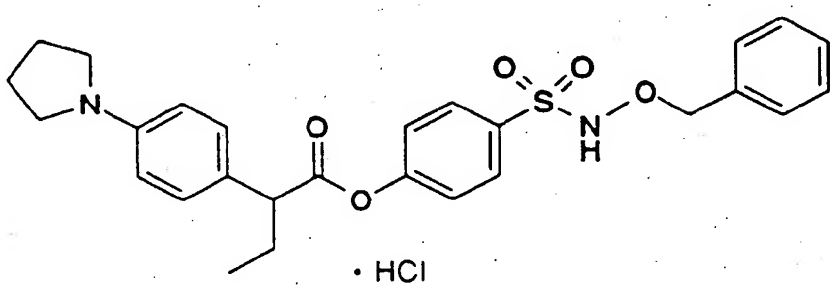


NMR ($CDCl_3$): δ 7.80 (2H, d, J=8.6Hz), 7.20 (2H, d, J=8.8Hz), 7,11 (2H, d, J=8.6Hz), 6.54 (2H, d, J=8.8Hz), 5.63 (1H, t, J=6.3Hz), 3.80-3.64 (1H, m), 3.62-3.41 (3H, m), 3.35-3.20 (4H, m), 3.10-2.80 (3H, m), 2.30-1.70 (7H, m), 0.96 (3H, t, J=7.4Hz);

TLC : Rf 0.28 (ethyl acetate:hexane=4:1).

Example 1(53)

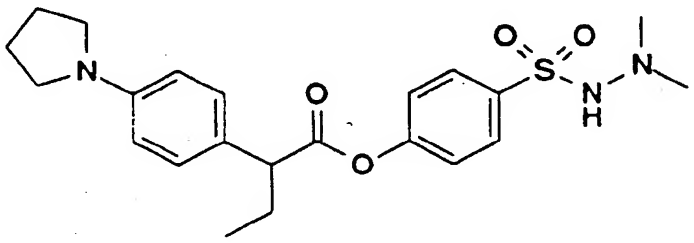
4-(N-benzyloxysulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ 7.87 (2H, d, J=8.8Hz), 7.32-7.12 (9H, m), 6.93 (1H, s), 6.54 (2H, d, J=8.8Hz), 4.94 (2H, s), 3.57 (1H, t, J=7.8Hz), 3.31-3.25 (4H, m), 2.25-1.80 (6H, m), 0.968 (3H, t, J=7.4Hz);
TLC : Rf 0.55 (hexane:ethyl acetate:acetic acid=5:2:0.2).

Example 1(54)

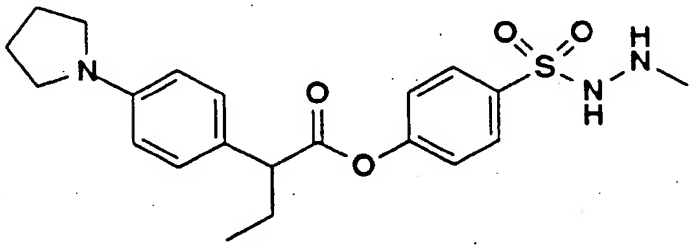
4-(N-(N',N'-dimethylamino)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.92 (2H, d, J=8.7Hz), 7.23 (2H, d, J=8.7Hz), 7.15 (2H, d, J=8.7Hz), 6.55 (2H, d, J=8.7Hz), 3.58 (1H, d, J=7.7Hz), 3.29 (4H, t, J=6.6Hz), 2.37 (6H, s), 2.25-1.75 (6H, m), 0.98 (3H, t, J=7.4Hz);
TLC : Rf 0.45 (hexane:ethyl acetate=1:1).

Example 1(55)

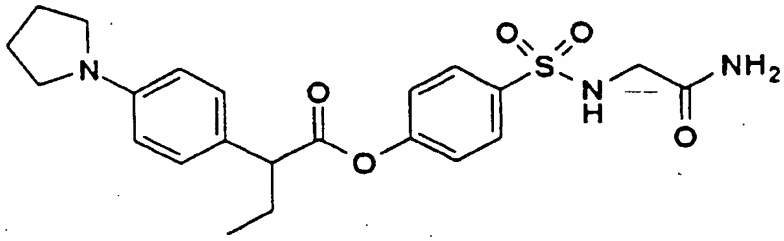
4-(N-(N'-methylamino)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.82 (2H, d, J=8.7Hz), 7.23 (4H, m), 6.56 (2H, d, J=8.6Hz), 3.60 (1H, m), 3.29 (4H, t, J=6.6Hz), 2.85 (3H, s), 2.25-1.80 (6H, m), 0.99 (3H, t, J=7.4Hz);
TLC : Rf 0.35 (hexane:ethyl acetate=1:1).

Example 1(56)

4-(N-(carbamoylmethyl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

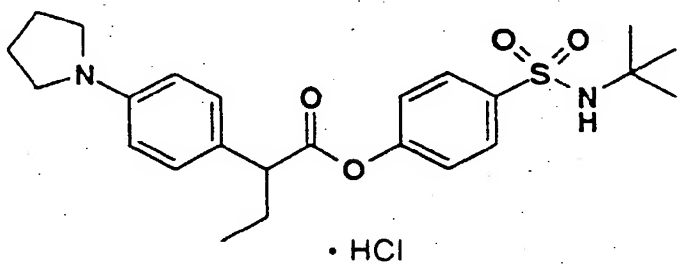


NMR ($CDCl_3$): δ 7.78 (2H, d, J=8.7Hz), 7.20 (2H, d, J=8.6Hz), 7.11 (2H, d, J=8.7Hz), 6.54 (2H, d, J=8.6Hz), 6.42-6.30 (1H, brs), 6.20-5.96 (2H, m), 3.58 (1H, t, J=7.8Hz), 3.50 (2H, s), 3.38-3.18 (4H, m), 2.26-1.74 (6H, m), 0.96 (3H, t, J=7.3Hz);

TLC : Rf 0.41 (chloroform:methanol=9:1).

Example 1(57)

4-(N-t-butylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



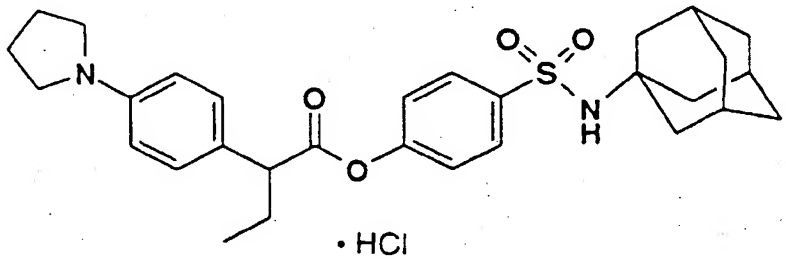
· HCl

NMR ($CDCl_3$): δ 7.89 (2H, d, J=8.8Hz), 7.63 (2H, d, J=8.6Hz), 7.48 (2H, d, J=8.6Hz), 7.12 (2H, d, J=8.8Hz), 4.83 (1H, s), 3.74 (1H, t, J=7.6Hz), 3.80-3.50 (4H, m), 2.40-2.25 (4H, m), 2.40-2.10 and 2.05-1.75 (each 1H, m), 1.22 (9H, s), 1,00 (3H, t, J=7.4Hz);

TLC : Rf 0.55 (ethyl acetate:hexane=1:2).

Example 1(58)

4-(N-adamantan-1-ylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



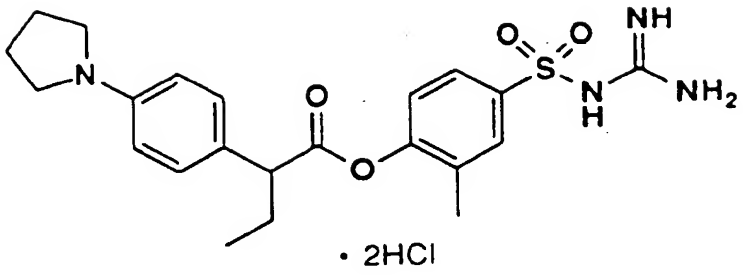
· HCl

NMR ($CDCl_3$): δ 7.89 (2H, d, J=8.6Hz), 7.60-7.45 (4H, m), 7.12 (2H, d, J=8.6Hz), 4.64 (1H, brs, NH), 3.80-3.55 (5H, m), 2.40-1.48 (21H, m), 0.999 (3H, t, J=7.2Hz);

TLC : Rf 0.44 (hexane:ethyl acetate:acetic acid=5:2:0.2).

Example 1(59)

4-guanidinosulfonyl-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

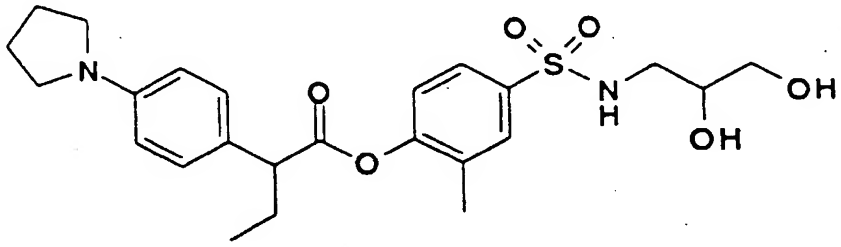


• 2HCl

NMR (DMSO-d_6): δ 7.66-7.53 (2H, m), 7.28 (2H, d, J=8.0Hz), 7.04 (1H, d, J=8.0Hz), 7.10-6.50 (6H, m), 3.76 (1H, t, J=7.5Hz), 3.50-3.20 (4H, m), 2.20-1.70 (2H, m), 2.10-1.90 (4H, m), 1.93 (3H, s), 0.91 (3H, t, J=7.5Hz);
TLC : Rf 0.36 (water:methanol:chloroform=1:10:90).

Example 1(60)

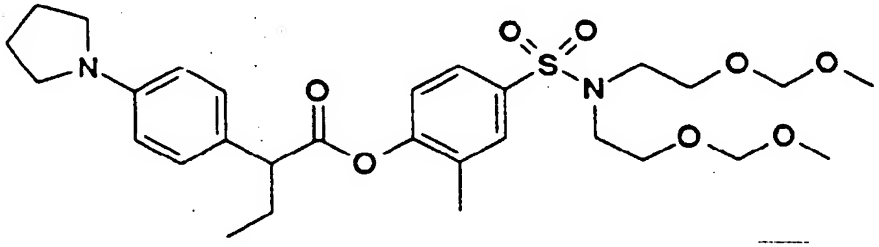
4-(N-2RS,3-dihydroxypropylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 7.70-7.60 (2H, m), 7.47 (1H, t, J=6.0Hz), 7.18 (2H, d, J=8.5Hz), 7.13 (1H, d, J=8.5Hz), 6.55 (2H, d, J=8.5Hz), 3.70 (1H, t, J=7.5Hz), 3.55-3.35 (6H, m), 2.94-2.78 (1H, m), 2.66-2.54 (1H, m), 2.25-1.60 (2H, m), 2.05-1.90 (4H, m), 1.96 (3H, s), 0.91 (3H, t, J=7.5Hz);
TLC : Rf 0.29 (water:methanol:chloroform=1:10:90).

Example 1(61)

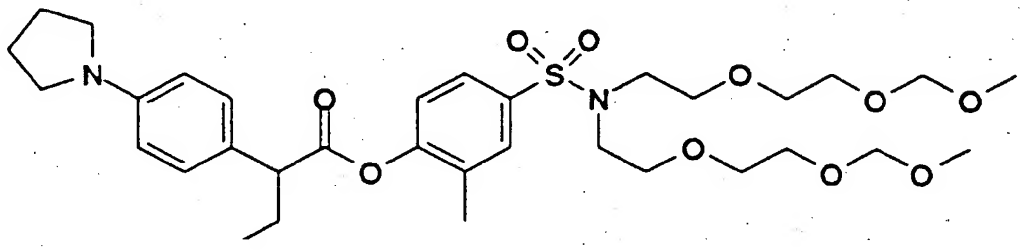
4-(N,N-bis(2-(methoxymethoxy)ethyl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70-7.58 (2H, m), 7.22 (2H, d, J=9Hz), 7.03 (1H, d, J=8Hz), 6.55 (2H, d, J=9Hz), 4.54 (4H, s), 3.67 (4H, t, J=6Hz), 3.60 (1H, t, J=7Hz), 3.43 (4H, t, J=6Hz), 3.35-3.20 (10H, m), 2.30-1.75 (9H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.27 (hexane:ethyl acetate=2:1).

Example 1(62)

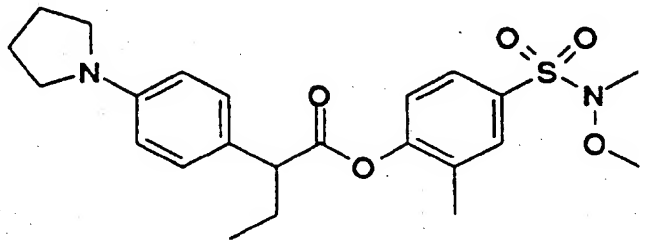
4-(N,N-bis(2-(2-(methoxymethoxy)ethoxy)ethyl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.68-7.58 (2H, m), 7.22 (2H, d, J=9Hz), 7.03 (1H, d, J=8Hz), 6.55 (2H, d, J=9Hz), 4.63 (4H, s), 3.70-3.50 (13H, m), 3.45-3.20 (8H, m), 3.35 (6H, s), 2.30-1.75 (9H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.20 (hexane:ethyl acetate=1:1).

Example 1(63)

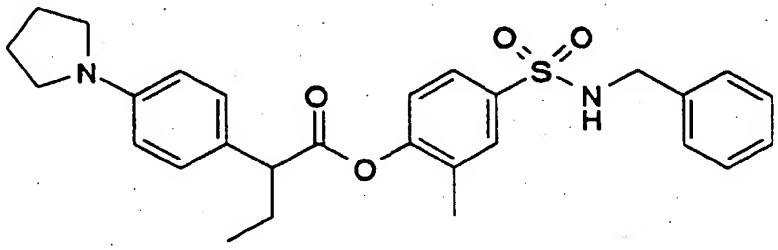
4-(N-methyl-N-methoxysulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.68 (1H, s), 7.66 (1H, d, J=8.4Hz), 7.22 (2H, d, J=8.6Hz), 7.11 (1H, d, J=8.4Hz), 6.55 (2H, d, J=8.6Hz), 3.78 (3H,s), 3.62 (1H, t, J=7.7Hz), 3.28 (4H, t, J=6.6Hz), 2.76 (3H, s), 2.3-2.1 (1H, m), 2.06 (3H, s), 2.1-1.9 (4H, m), 2.1-1.8 (1H, m), 0.99 (3H, t, J=7.3Hz);
TLC : Rf 0.36 (hexane:ethyl acetate=4:1).

Example 1(64)

4-(N-benzylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

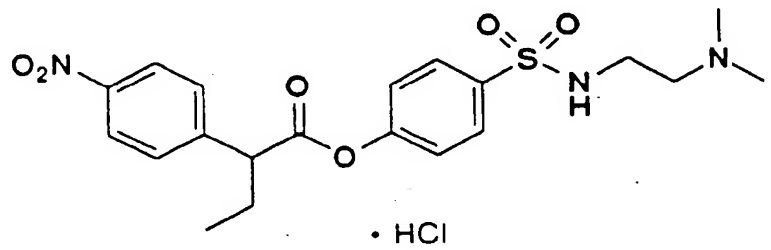


NMR ($CDCl_3$): δ 7.66-7.62 (2H, m), 7.29-7.15 (7H, m), 7.05 (1H, d, J=9.0Hz), 6.55 (2H, d, J=8.6Hz), 4.65 (1H, t, J=5.6Hz), 4.11 (2H, d, J=5.6Hz), 3.62 (1H, t, J=7.8Hz), 3.33-3.26 (4H, m), 2.27-1.82 (6H, m), 2.00 (3H, s), 1.00 (3H, t, J=7.4Hz);

TLC : Rf 0.86 (hexane:ethyl acetate=1:1).

Example 1(65)

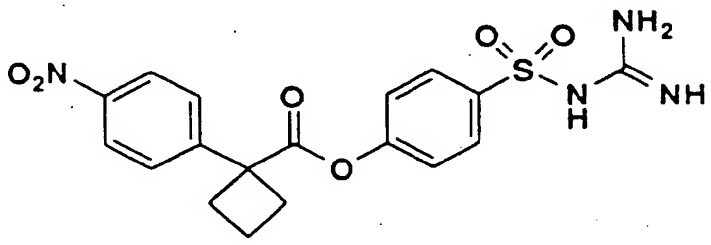
4-(N-2-(N',N'-dimethylamino)ethylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 8.27 (2H, d, J=8.5Hz), 7.93 (2H, d, J=8.5Hz), 7.68 (2H, d, J=8.5Hz), 7.28 (2H, d, J=8.5Hz), 4.04 (1H, t, J=7.6Hz), 3.22 (4H, m), 2.93 (6H, s), 2.28 (1H, ml, 1.97 (1H, m), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.39 (chloroform:methanol:water=9:1:0.1).

Example 1(66)

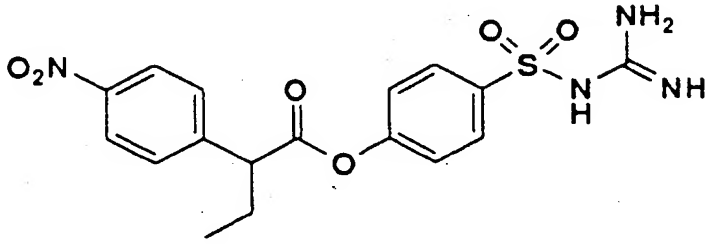
4-guanidinosulfonylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR ($CDCl_3$): δ 8.26 (2H, d, J=8.8Hz), 7.85 (2H, d, J=8.8Hz), 7.57 (2H, d, J=8.8Hz), 7.04 (2H. d, J=8.8Hz), 6.34 (1H, brs), 3.14-2.96 (2H, m), 2.77-2.59 (2H, m), 2.38-1.90 (2H, m);
TLC : Rf 0.56 (acetic acid:methanol:chloroform=1:5:25).

Example 1(67)

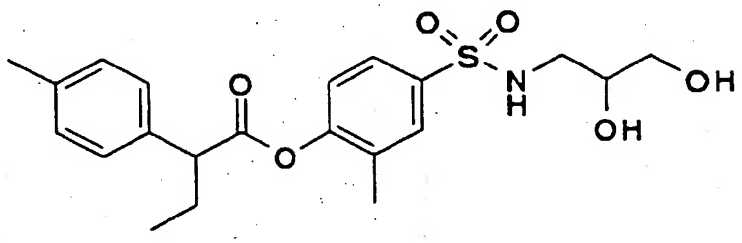
4-guanidinosulfonylphenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR ($DMSO-d_6$): δ 8.27 (2H, d, J=8.8Hz), 7.78 (2H, d, J=8.8Hz), 7.71 (2H, d, J=8.8Hz), 7.19 (2H, d, J=8.8Hz), 7.0-6.4 (4H, brs), 4.15 (1 H, t, J=7.6Hz), 2.30-2.05 and 2.05-1.75 (each 1H, m), 0.92 (3H, t, J=7.6Hz);
TLC : Rf 0.09 (acetic acid:methanol:chloroform=1:2:40).

Example 1(68)

4-(N-2RS,3-dihydroxypropylsulfamoyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester

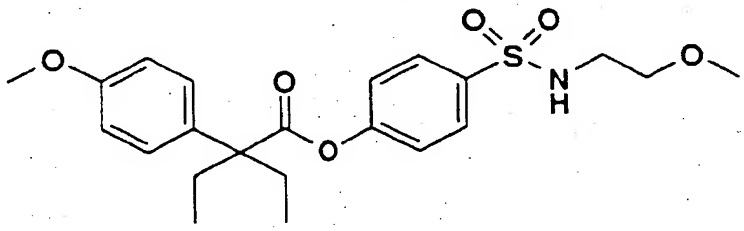


NMR ($CDCl_3$): δ 7.67-7.61 (2H, m), 7.27 (2H, d, J=8Hz), 7.17 (2H, d, J=8Hz), 7.04 (1H, d, J=8Hz), 5.54 (1H, br), 3.80-3.46 (3H, m), 3.42 (1H, br), 3.70 (1H, t, J=8Hz), 3.11-2.87 (2H, m), 2.83 (1H, br), 2.35 (3H, s), 2.32-2.11 and 2.03-1.79 (each 1H, m), 1.98 (3H, s), 0.99 (3H, t, J=8Hz);

TLC : Rf 0.40 (chloroform:methanol:water=9:1:0.1).

Example 1(69)

4-(N-2-methoxyethylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester

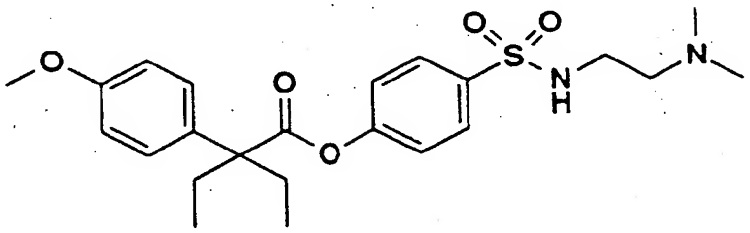


NMR ($CDCl_3$): δ 7.83 (2H, d, J=8.8Hz), 7.27 (2H, d, J=8.8Hz), 7.08 (2H, d, J=9.2Hz), 6.90 (2H, d, J=8.8Hz), 4.92 (1H, t, J=6.5Hz), 3.82 (3H, s), 3.38 (2H, t, J=5.4Hz), 3.25 (3H, s), 3.11 (2H, t, J=6.0Hz), 2.28-2.04 (4H, m), 0.846 (6H, t, J=7.4Hz);

TLC : Rf 0.16 (hexane:ethyl acetate=2:1).

Example 1(70)

4-(N-2-(N',N'-dimethylamino)ethylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester · acetate



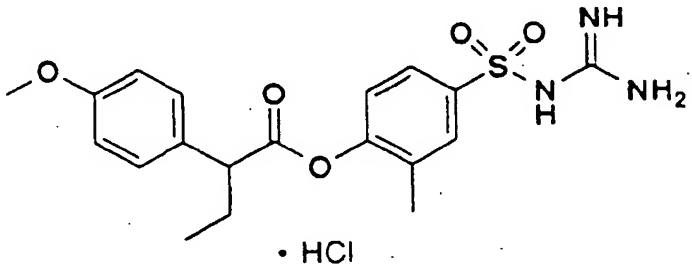
· CH_3COOH

NMR ($CDCl_3$): δ 7.85 (2H, d, J=8.6Hz), 7.28 (2H, d, J=8.8Hz), 7.09 (2H, d, J=8.6Hz), 6.92 (2H, d, J=8.8Hz), 3.83 (3H, s), 2.53-2.47 (4H, m), 2.24 (6H, s), 2.24-2.11 (4H, m), 0.847 (6H, t, J=7.4Hz);

TLC : Rf 0.26 (chloroform:methanol:water=25:5:1).

Example 1(71)

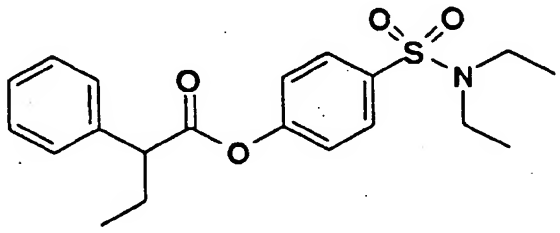
4-(guanidinosulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 7.62 (1H, s), 7.60 (1H, d, J=8.0Hz), 7.30 (2H, d, J=8.5Hz), 6.96 (1H, d, J=8.0Hz), 6.90 (2H, d, J=8.5Hz), 6.6-6.1 (4H, brs), 3.80 (1H, t, J=7.5Hz), 2.3-2.0 and 2.0-1.7 (each 1H, m), 1.65 (3H, s), 0.98 (3H, t, J=7.5Hz);
TLC : Rf 0.60 (water:methanol:chloroform=1:10:40).

Example 1(72)

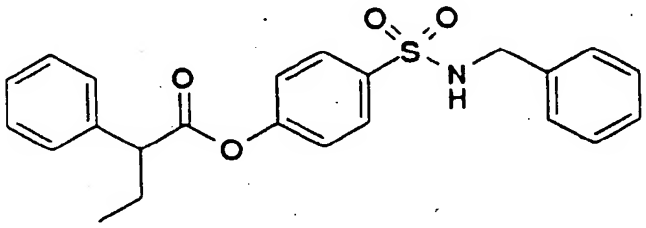
4-(N,N-diethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.83-7.73 (2H, m), 7.40-7.23 (5H, m), 7.16-7.07 (2H, m), 3.69 (1H, t, J=7Hz), 3.20 (4H, q, J=7Hz), 2.35-1.75 (2H, m), 1.11 (6H, t, J=7Hz), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.39 (hexane:ethyl acetate=7:3).

Example 1(73)

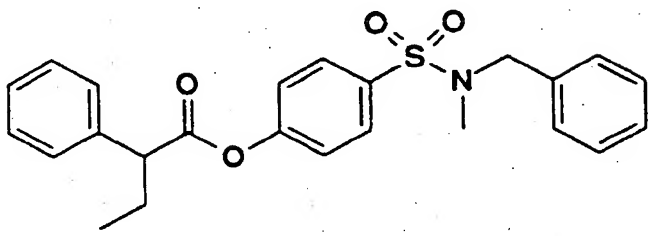
4-(N-benzylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.89-7.79 (2H, m), 7.42-7.08 (12H, m), 4.61 (1H, t, J=7Hz), 4.13 (2H, d, J=7Hz), 3.70 (1H, t, J=7Hz), 2.36-2.11 (1H, m), 2.05-1.80 (1H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.41 (hexane:ethyl acetate=2:1).

Example 1(74)

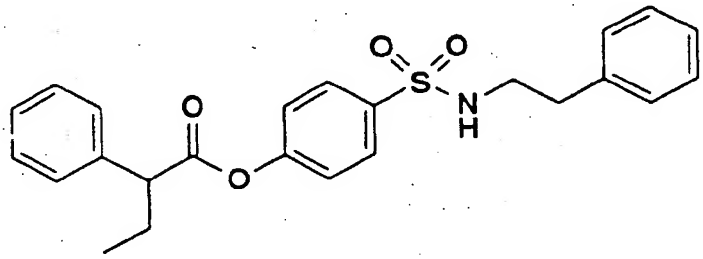
4-(N-methyl-N-benzylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.86-7.76 (2H, m), 7.43-7.14 (12H, m), 4.11 (2H, s), 3.73 (1H, t, J=7Hz), 2.59 (3H, s), 2.38-2.13 (1H, m), 2.06-1.81 (1H, m), 1.01 (3H, t, J=7Hz);
TLC : Rf 0.57 (hexane:ethyl acetate=2:1).

Example 1(75)

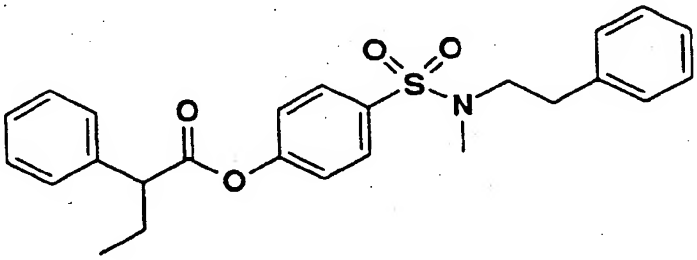
4-(N-2-phenylethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.81-7.71 (2H, m), 7.43-7.03 (12H, m), 4.40 (1H, t, J=7Hz), 3.71 (1H, t, J=7Hz), 3.21 (2H, q, J=7Hz), 2.76 (2H, t, J=7Hz), 2.24 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.93 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.00 (3H, t, J=7Hz);
TLC : Rf 0.46 (hexane:ethyl acetate=3:2).

Example 1(76)

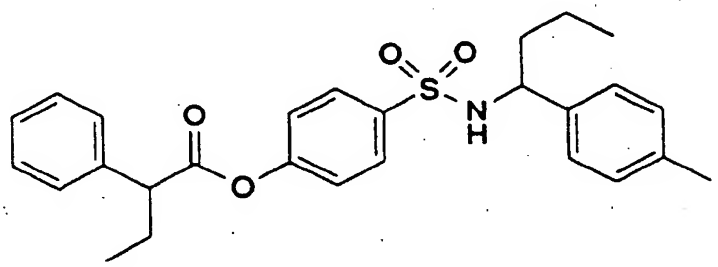
4-(N-methyl-N-2-phenylethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.77-7.68 (2H, m), 7.41-7.08 (12H, m), 3.71 (1H, t, J=7Hz), 3.33-3.18 (2H, m), 2.92-2.79 (2H, m), 2.73 (3H, s), 2.24 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.92 (1H, ddq, J=14Hz, 7Hz, 7Hz), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.32 (hexane:ethyl acetate=3:2).

Example 1(77)

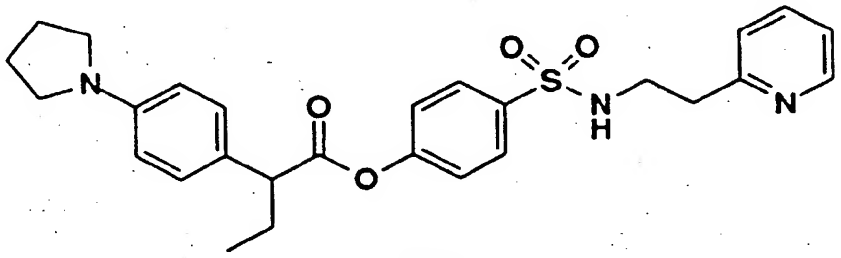
4-(N-1RS-(4-methylphenyl)butylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.55 (2H, d, J=8Hz), 7.41-7.23 (5H, m), 6.98-6.78 (6H, m), 4.81 (1H, d, J=7Hz), 4.23 (1H, q, J=7Hz), 3.68 (1H, t, J=7Hz), 2.35-2.08 (1H, m), 2.20 (3H, s), 1.91 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.79-1.52 (2H, m), 1.36-1.06 (2H, m), 0.99 (3H, t, J=7Hz), 0.83 (3H, t, J=7Hz);
TLC : Rf 0.15 (hexane:ethyl acetate=4:1).

Example 1(78)

4-(N-2-(pyridin-2-yl)ethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

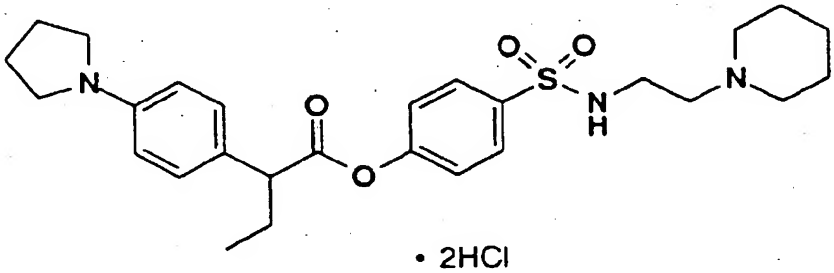


• 2HCl

NMR (DMSO-d_6): δ 8.79 (1H, d, J=5.0Hz), 8.50 (1H, t, J=7.4Hz), 8.04 (1H, m), 7.90 (2H, m), 7.79 (2H, d, J=8.6Hz), 7.28 (2H, m), 7.21 (2H, d, J=8.4Hz), 6.90 (2H, m), 3.76 (1H, t, J=7.0Hz), 3.34 (4H, brs), 3.23 (4H, brs), 2.01 (5H, m), 1.80 (1H, m), 0.91 (3H, t, J=7.0Hz);
TLC : Rf 0.48 (chloroform:methanol:water=9:1:0.1).

Example 1(79)

4-(N-2-(piperidin-1-yl)ethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

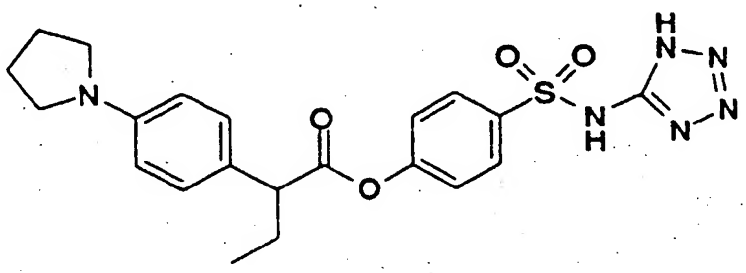


• 2HCl

NMR (CD_3OD): δ 7.92 (2H, d, J=8.8Hz), 7.71 (2H, d, J=8.8Hz), 7.63 (2H, d, J=8.8Hz), 7.26 (2H, d, J=8.8Hz), 3.95 (1H, t, J=7.2Hz), 3.81 (4H, m), 3.55 (2H, brd, J=12.0Hz), 3.24 (4H, brs), 2.98 (2H, brt, J=12.0Hz), 2.32 (4H, m), 1.89 (7H, m), 1.55 (1H, m), 0.99 (3H, t, J=7.2Hz);
TLC : Rf 0.39 (chloroform:methanol:water=9:1:0.1).

Example 1(80)

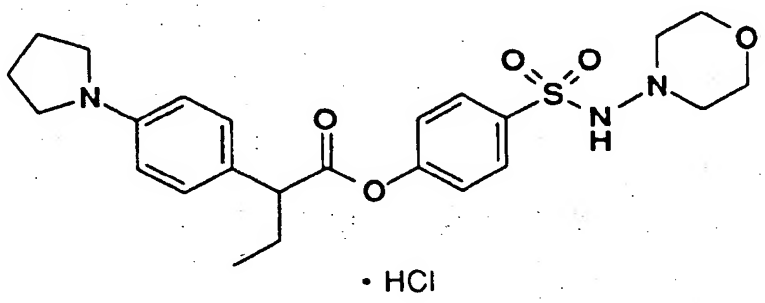
4-(N-(tetrazol-5-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (CD_3OD): δ 7.89 (2H, d, J=8.6Hz), 7.15 (2H, d, J=8.6Hz), 7.02 (2H, d, J=8.6Hz), 6.55 (2H, d, J=8.6Hz), 3.58 (1H, t, J=7.8Hz), 3.35-3.15 (4H, m), 2.20-1.95 and 1.95-1.70 (each 1H, m), 2.05-1.95 (4H, m), 0.93 (3H, t, J=7.2Hz);
TLC : Rf 0.46 (acetic acid:methanol:chloroform=1:5:25).

Example 1(81)

4-(N-(morpholin-4-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

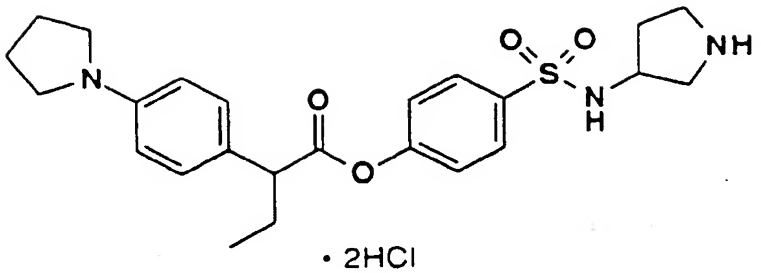


• HCl

NMR ($CDCl_3$): δ 7.97 (2H, d, J=8.6Hz), 7.61 (2H, d-like), 7.48 (2H, d-like), 7.16 (2H, d, J=8.6Hz), 5.99 (1H, s), 3.74 (1H, t, J=7.8Hz), 3.76-3.63 (4H, m), 3.65-3.54 (4H, m), 2.70-2.58 (4H, m), 2.42-2.29 (4H, m), 2.37-2.10 and 2.04-1.77 (each 1H, m), 1.00 (3H, t, J=7.2Hz);
TLC : Rf 0.45 (methanol:chloroform=1:20).

Example 1(82)

4-(N-(pyrrolidin-3-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

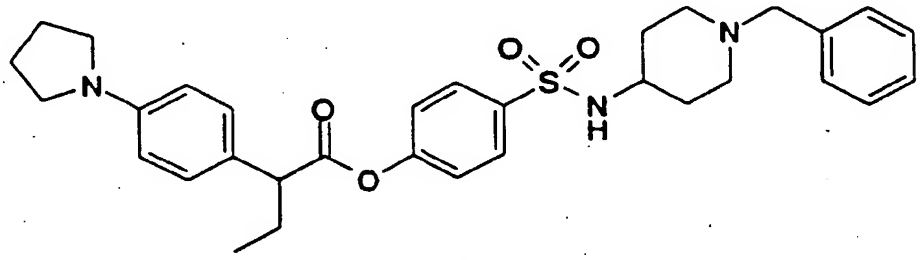


• 2HCl

NMR ($CDCl_3$): δ 7.7-7.5 (4H, m), 7.42 (2H, d, J=8.6Hz), 6.96 and 6.92 (2H, d, J=8.6Hz), 4.35-4.13 (1H, m), 3.5-2.9 (10H, m), 2.40-2.25 (4H, m), 2.20-1.55 (4H, m), 0.94 (3H, t, J=7.2Hz);
TLC : Rf 0.35 (methanol:chloroform=1:10).

Example 1(83)

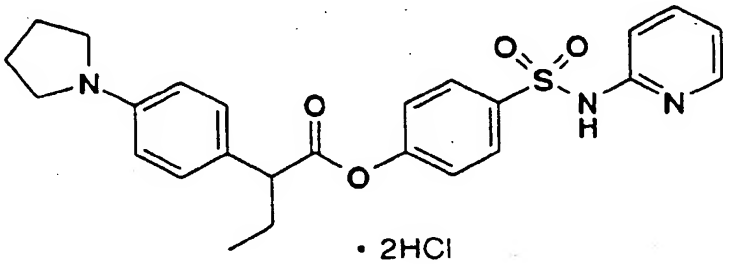
4-(N-(1-benzylpiperidin-4-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.82 (2H, d, J=9.0Hz), 7.36-7.08 (5H, m), 7.21 (2H, d, J=9.0Hz), 7.13 (2H, d, J=8.8Hz), 6.55 (2H, d, J=8.8Hz), 4.50 (1H, d, J=5.7Hz), 3.58 (1H, t, J=5.0Hz), 3.43 (2H, s), 3.36-3.21 (4H, m), 3.21-3.02 (1H, m), 2.78-2.61 (2H, m), 2.28-1.65 (10H, m), 1.56-1.34 (1H, m), 0.97 (3H, t, J=7.2Hz);
TLC : Rf 0.60 (ethyl acetate:hexane=9:1).

Example 1(84)

4-(N-(pyridin-2-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

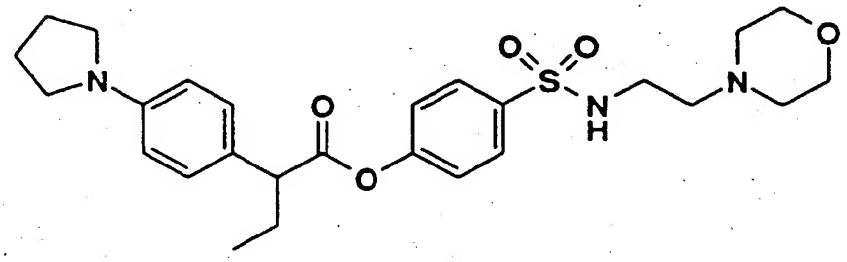


• 2HCl

NMR ($CDCl_3$): δ 8.26 (1 H, d, J=6.0Hz), 7.96 (2H, d, J=8.6Hz), 7.83 (1H, t, J=8.6Hz), 7.72 (2H, d, J=8.6Hz), 7.55 (1H, d, J=8.6Hz), 7.48 (2H, d, J=8.6Hz), 7.12 (2H, d, J=8.6Hz), 6.95 (1H, t, J=6.0Hz), 3.74 (1H, t, J=7.6Hz), 3.80-3.60 (4H, m), 2.44-2.24 (4H, m), 2.32-2.02 and 2.02-1.72 (each 1H, m), 0.97 (3H, t, J=7.2Hz);
TLC : Rf 0.51 (ethyl acetate:hexane=2:1).

Example 1(85)

4-(N-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

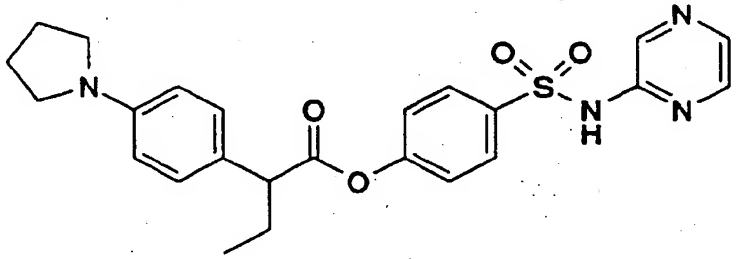


NMR ($CDCl_3$): δ 7.83 (2H, d, J=8.9Hz), 7.21 (2H, d, J=8.7Hz), 7.13 (2H, d, J=8.9Hz), 6.55 (2H, d, J=8.7Hz), δ 23-5 06 (1H, brs), 3.64-3.52 (5H, m), 3.36-3.20 (4H, m), 2.98 (2H, t, J=6.0Hz), 2.38 (2H, t, J=6.0Hz), 2.30-2.20 (4H, m) 2 20-1.70 (6H, m), 0.97 (3H, t, J=7.2Hz);

TLC . Rf 0.24 (ethyl acetate:hexane=7:3).

Example 1(86)

4-(N-(pyrazin-2-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 3hydrochloride



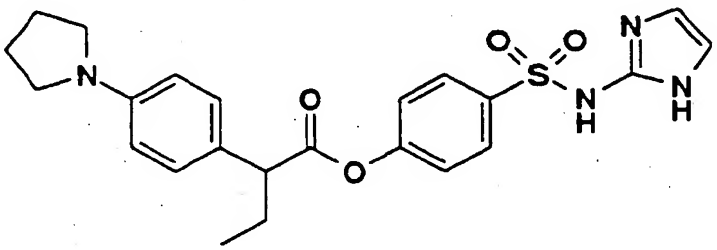
• 3HCl

NMR ($CDCl_3$): δ 8.46 (1H, s), 8.17 (2H, s), 8.01 (2H, d, J=8.2Hz), 7.7-7.4 (4H, m), 7.14 (2H, d, J=8.2Hz), 3.9-3.5 (5H, m), 2.5-2.2 (4H, m), 2.4-2.1 and 2.1-1.8 (each 1 H, m), 0.98 (3H, t, J=7.2Hz);

TLC : Rf 0.18 (hexane:ethyl acetate=1:1).

Example 1(87)

4-(N-(imidazol-2-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

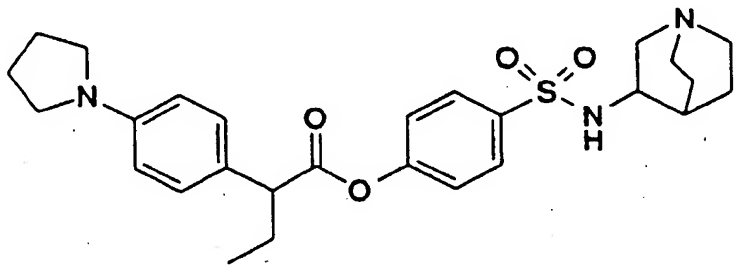


NMR ($CDCl_3$): δ 7.90 (2H, d, J=8.8Hz), 7.19 (4H, d, J=8.8Hz), 6.81 (1H, d, J=2.0Hz), 6.54 (1H, d, J=2.0Hz), 6.54 (2H, d, J=8.8Hz), 3.57 (1H, t, J=7.8Hz), 3.28 (4H, t-like), 2.30-2.00 and 2.00-1.70 (each 1H, m), 2.00 (4H, t-like), 0.96 (3H, t, J=7.4Hz);

TLC : Rf 0.67 (methanol:chloroform=1:10).

Example 1(88)

4-(N-(quinuclidin-3RS-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

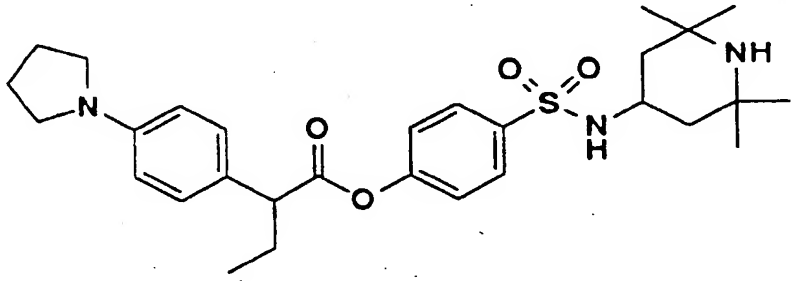


NMR ($CDCl_3$): δ 7.88 (2H, d, J=8.8Hz), 7.21 (2H, d, J=8.8Hz), 7.11 (2H, d, J=8.8Hz), 6.55 (2H, d, J=8.8Hz), 3.58 (1H, t, J=7.6Hz), 3.60-3.47 (1H, m), 3.35-3.20 (4H, m), 3.30-2.80 (6H, m), 2.10-1.95 (4H, m), 2.30-1.40 (7H, m), 0.98 (3H, t, J=7.2Hz);

TLC : Rf 0.43 (acetic acid:methanol:chloroform=1:5:25).

Example 1(89)

4-(N-(2,2,6,6-tetramethylpiperidin-4-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

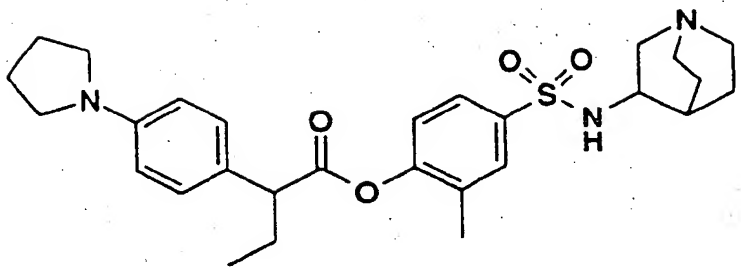


NMR ($CDCl_3$+CD_3OD): δ 7.85 (2H, d, J=8.8Hz), 7.22 (2H, d, J=8.6Hz), 7.14 (2H, d, J=8.8Hz), 6.57 (2H, d, J=8.6Hz), 3.59 (1H, t, J=7.8Hz), 3.60-3.42 (1H, m), 3.35-3.20 (4H, m), 2.30-1.75 (2H, m), 2.06-1.96 (4H, m), 1.63 (2H, dd, J=13.2 and 3.8Hz), 1.33-1.08 (2H, m), 1.19 (12H, s), 0.98 (3H, t, J=7.3Hz);

TLC : Rf 0.55 (chloroform:methanol:acetic acid=25:5:1).

Example 1(90)

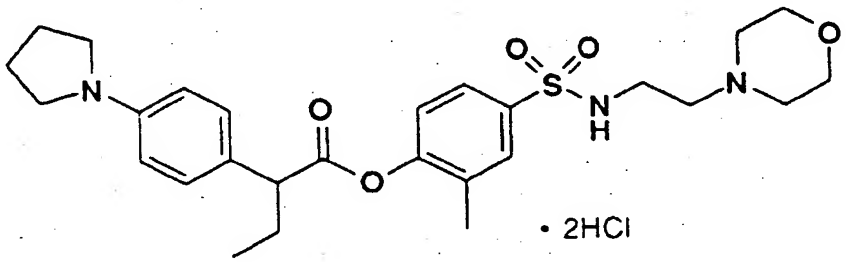
4-(N-(quinuclidin-3RS-yl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.69 (1H, d, J=2Hz), 7.66 (1H, dd, J=8 and 2Hz), 7.30-7.13 (2H, m), 7.06 (1H, d, J=8Hz), 6.55 (2H, d, J=9Hz), 3.62 (1H, t, J=8Hz), 3.38-3.23 (5H, m), 3.23-3.05 (1H, m), 2.90-2.48 (5H, m), 2.32-2.08 (1H, m), 2.04 (3H, s), 2.08-1.03 (10H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.43 (chloroform:methanol:water=8:2:0.2).

Example 1(91)

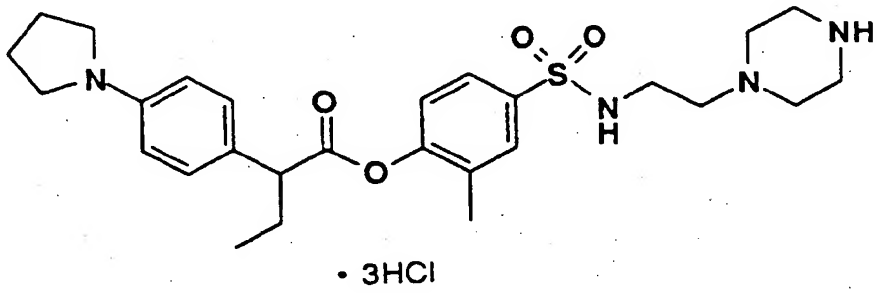
4-(N-2-(morpholin-4-yl)ethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (DMSO-d_6): δ 11.3-11.1 (1H, brs), 8.18 (1H, brs), 7.75 (1H, s), 7.70 (1H, d, J=8.0Hz), 7.27 (2H, d, J=8.6Hz), 7.18 (2H, d, J=9.2Hz), 4.0-3.7 (5H, m), 3.4-3.0 (12H, m), 2.2-2.0 (1H, m), 2.1-1.9 (4H, brs), 2.0-1.7 (1H, m), 1.98 (3H, s), 0.91 (3H, t, J=7.3Hz);
TLC : Rf 0.50 (chloroform:methanol=9:1).

Example 1(92)

4-(N-2-(piperazin-4-yl)ethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 3hydrochloride

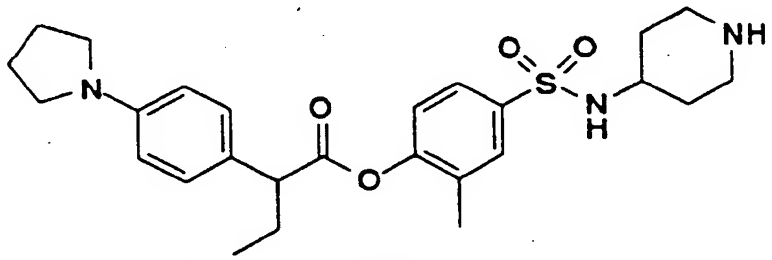


NMR (DMSO-d_6): δ 9.6-9.2 (2H, br), 7.71 (1H, s), 7.67 (1H, d, J=8.0Hz), 7.18 (2H, d, J=8.4Hz), 7.14 (1H, d,

J=8.0Hz), 6.53 (2H, d, J=8.4Hz), 3.69 (1H, t, J=7.3Hz), 3.7-2.6 (16H, br), 2.2-2.0 (1H, m), 2.0-1.9 (4H, brs), 1.96 (3H, s), 1.9-1.7 (1H, m), 0.90 (3H, t, J=7.1Hz);
TLC : Rf 0.46 (chloroform:methanol:acetic acid=25:5:1).

Example 1(93)

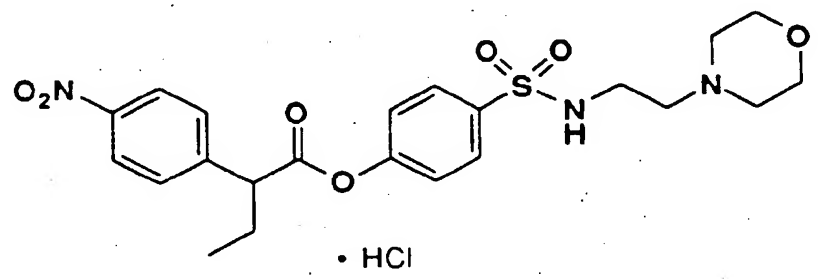
4-(N-(piperidin-4-yl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (DMSO-d_6): δ 9.1-8.7 (1H, br), 8.00 (1H, d, J=7.2Hz), 7.71 (1H, s), 7.68 (1H, d, J=8.4Hz), 7.26 (2H, d, J=8.4Hz), 7.15 (1H, d, J=8.4Hz), 6.79 (2H, d, J=8.4Hz), 3.76 (1H, t, J=7.8Hz), 3.4-3.2 (4H, brs), 3.2-3.0 (3H, br), 3.0-2.7 (2H, br), 2.2-1.9 (1H, m), 1.99 (4H, brs), 1.97 (3H, s), 1.9-1.5 (5H, m), 0.91 (3H, t, J=7.3Hz);
TLC : Rf 0.46 (chloroform:methanol:acetic acid=25:5:1).

Example 1(94)

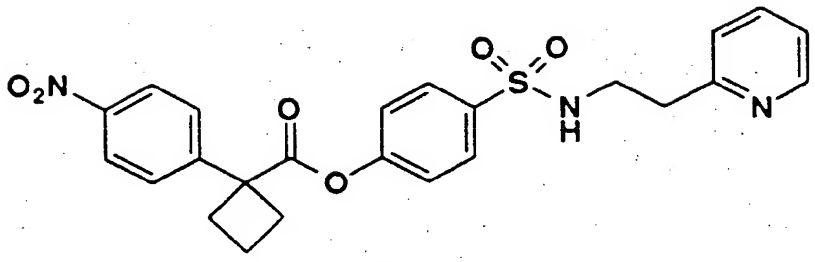
4-(N-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 8.27 (2H, d, J=8.6Hz), 7.92 (2H, d, J=9.0Hz), 7.67 (2H, d, J=8.6Hz), 7.27 (2H, d, J=9.0Hz), 4.03 (1H, t, J=7.6Hz), 3.90 (2H, m), 3.50 (2H, m), 3.28 (8H, m), 2.28 (1H, m), 1.99 (1H, m), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.61 (chloroform:methanol:water=9:1:0.1).

Example 1(95)

4-(N-2-(pyridin-2-yl)ethylsulfamoyl)phenyl)1-(4-nitrophenyl)cyclobutanecarboxylic acid ester · hydrochloride

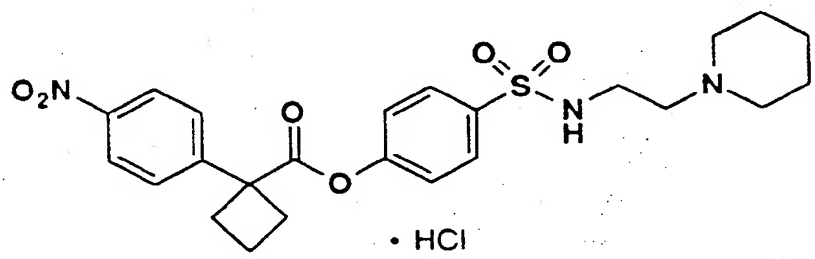


• HCl

NMR (CD_3OD): δ 8.72 (1H, d, J=8.0Hz), 8.53 (1H, t, J=8.0Hz), 8.28 (2H, d, J=8.6Hz), 7.96 (1H, d, J=8.0Hz), 7.93 (1H, d, J=8.0Hz), 7.79 (2H, d, J=8.6Hz), 7.66 (2H, d, J=8.6Hz), 7.17 (2H, d, J=8.6Hz), 3.30 (4H, m), 3.06 (2H, m), 2.72 (2H, m), 2.23 (1H, m), 2.04 (1H, m);
TLC : Rf 0.54 (chloroform:methanol:water=9:1:0.1).

Example 1(96)

4-(N-2-(piperidin-1-yl)ethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester · hydrochloride

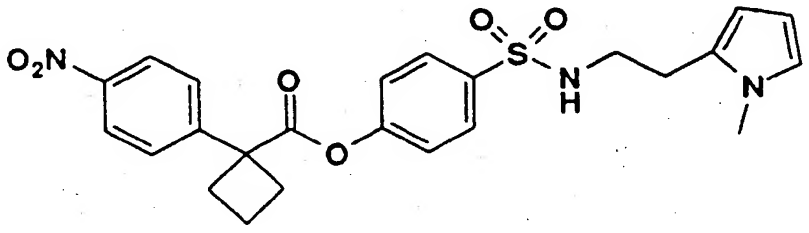


• HCl

NMR (CD_3OD): δ 8.28 (2H, d, J=8.4Hz), 7.90 (2H, d, J=8.4Hz), 7.66 (2H, d, J=8.4Hz), 7.23 (2H, d, J=8.4Hz), 3.50 (2H, m), 3.30 (4H, m), 3.06 (4H, m), 2.73 (2H, m), 2.22 (1H, m), 1.99 (1H, m), 1.87 (6H, m);
TLC : Rf 0.45 (chloroform:methanol:water=9:1:0.1).

Example 1(97)

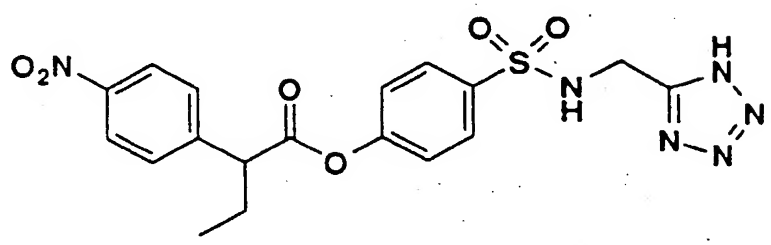
4-(N-2-(1-methylpyrrol-2-yl)ethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR ($CDCl_3$): δ 8.26 (2H, d, J=9.0Hz), 7.78 (2H, d, J=9.0Hz), 7.56 (2H, d, J=9.0Hz), 7.09 (2H, d, J=9.0Hz), 6.52 (1H, dd, J=2.0, 2.4Hz), 6.01 (1H, dd, J=2.4, 2.6Hz), 5.80 (1H, m), 4.64 (1H, t, J=6.6Hz), 3.42 (3H, s), 3.16 (2H, q, J=6.6Hz), 3.05 (2H, m), 2.74 (2H, t, J=6.6Hz), 2.66 (2H, m), 2.25 (1H, m), 2.03 (1H, m);
TLC : Rf 0.26 (hexane:ethyl acetate=2:1).

Example 1(98)

4-(N-(tetrazol-5-ylmethyl)sulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester

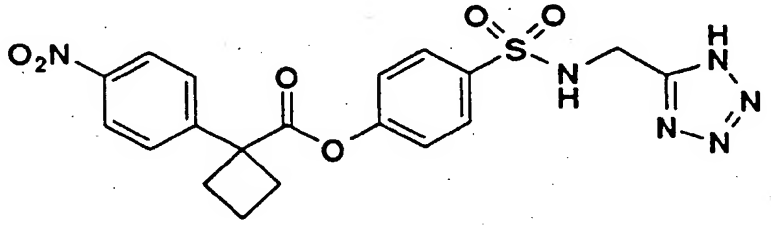


NMR (DMSO-d_6): δ 8.54 (1H, t, J=5.8Hz), 8.28 (2H, d, J=8.8Hz), 7.85 (2H, d, J=8.8Hz), 7.73 (2H, d, J=8.8Hz), 7.32 (2H, d, J=8.8Hz), 4.30 (2H, d, J=5.8Hz), 4.17 (1H, t, J=7.6Hz), 2.35-2.05 and 2.03-1.75 (each 1H, m), 0.92 (3H, t, J=7.2Hz);

TLC : Rf 0.45 (acetic acid:methanol:chloroform=1:5:25).

Example 1(99)

4-(N-(tetrazol-5-ylmethyl)sulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester

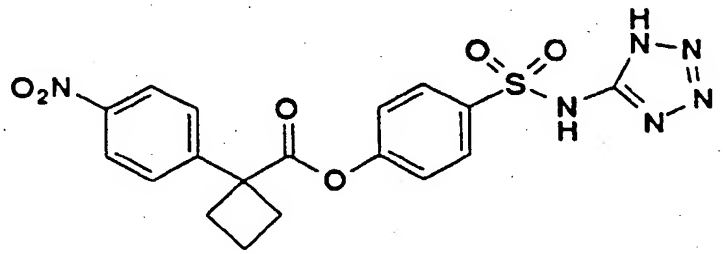


NMR (CD_3OD): δ 8.28 (2H, d, J=8.8Hz), 7.85 (2H, d, J=8.8Hz), 7.67 (2H,d, J=8.8Hz), 7.19 (2H, d, J=8.8Hz), 4.37 (2H, s), 3.16-2.96 (2H, m), 2.82-2.62 (2H, q-like), 2.37-2.12 and 2.12-1.90 (each 1H, m);

TLC : Rf 0.11 (acetic acid:methanol:chloroform=1:2:40).

Example 1(100)

4-(N-(tetrazol-5-yl)sulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester

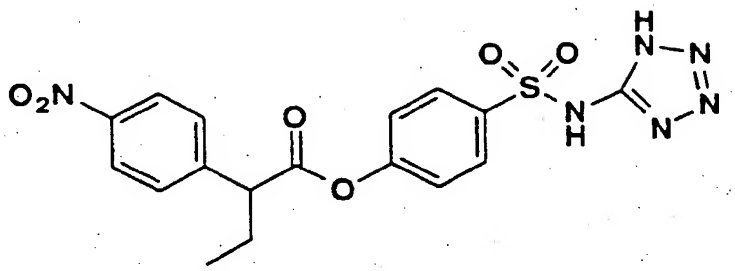


NMR (DMSO-d_6): δ 8.26 (2H, d, J=8.8Hz), 7.84 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.8Hz), 7.12 (2H, d, J=8.8Hz), 3.08-2.88 (2H, m), 2.74-2.54 (2H, q-like), 2.24-2.04 and 2.04-1.84 (each 1H, m);

TLC : Rf 0.29 (acetic acid:methanol:chloroform=1:5:25).

Example 1(101)

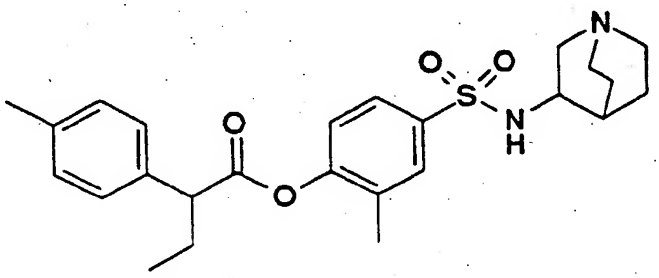
4-(N-(tetrazol-5-yl)sulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 13.88 (1H, brs), 8.26 (2H, d, J=8.8Hz), 7.82 (2H, d, J=8.8Hz), 7.70 (2H, d, J=8.8Hz), 7.06 (2H, d, J=8.8Hz), 4.12 (1H, t, J=7.4Hz), 2.30-2.00 and 2.00-1.70 (each 1H, m), 0.91 (3H, t, J=7.2Hz);
TLC : Rf 0.26 (acetic acid:methanol:chloroform=1:2:40).

Example 1(102)

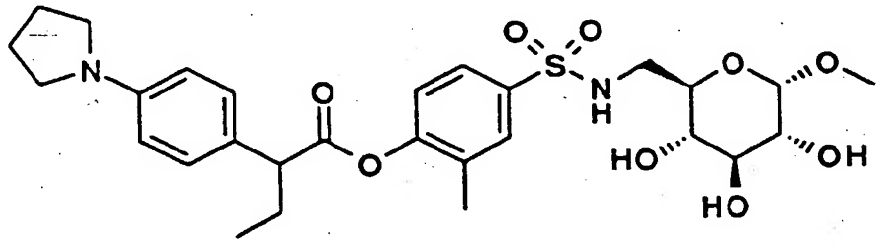
4-(N-(quinuclidin-3RS-yl)sulfamoyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70 (1H, d, J=2Hz), 7.67 (1H, dd, J=8 and 2Hz), 7.27 (2H, d, J=8Hz), 7.18 (2H, d, J=8Hz), 7.06 (1H, d, J=8Hz), 3.70 (1H, t, J=8Hz), 3.38-3.23 (1H, m), 3.23-3.05 (1H, m), 2.90-2.49 (5H, m), 2.36 (3H, s), 2.35-2.11 (1H, m), 2.00 (3H, s), 2.05-1.22 (6H, m), 1.00 (3H, t, J=7Hz);
TLC : Rf 0.40 (chloroform:methanol:water=8:2:0.2).

Example 1(103)

4-(N-2R-methoxy-3R-hydroxy-4S-hydroxy-5R-hydroxyperhydropyran-6R-ylmethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

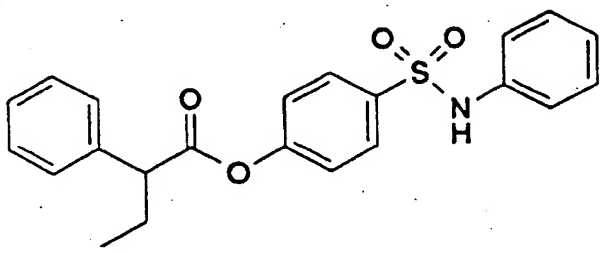


NMR ($CDCl_3$+6 drops of CD_3OD): δ 7.68-7.63 (m, 2H), 7.22 (d, J=8.8Hz, 2H), 7.05 (d, J=8.1Hz, 1H), 6.55 (d,

J=8.8Hz, 2H), 4.63 (d, J=3.7Hz, 1 H), 3.70-3.50 (m, 3H), 3.50-3.10 (m, 11H), 2.30-1.80 (m, 9H), 0.99 (t, J=7.4Hz, 3H);
TLC : Rf 0.41 (chloroform:methanol=8:1).

Example 1(104)

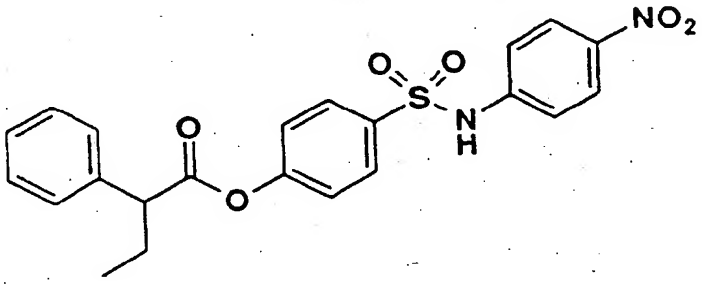
4-(N-phenylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.73 (2H, dd, J=2Hz, 8Hz), 7.40-7.16 (7H, m), 7.16-7.00 (5H, m), 6.76 (1H, s), 3.67 (1H, t, J=7Hz), 2.20 (1H, m), 1.89 (1H, m), 0.96 (3H, t, J=7Hz);
TLC : Rf 0.57 (hexane:ethyl acetate=1:1).

Example 1(105)

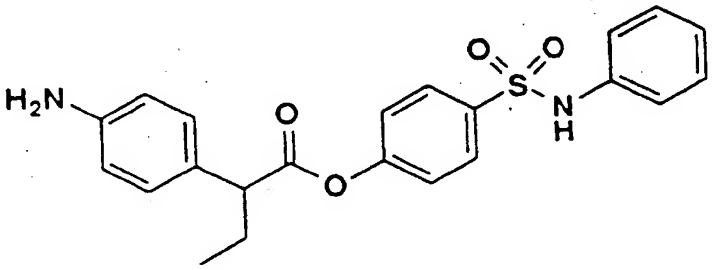
4-(N-4-nitrophenylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 8.10 and 7.85 (each 2H, dd, J=2Hz, 8Hz), 7.75 (1H, brs), 7.35 (5H, m), 7.20 and 7.14 (each 2H, dd, J=2Hz, J=8Hz), 3.69 (1H, t, J=7Hz), 2.20 and 1.90 (each 1 H, m), 0.96 (3H, t, J=7Hz);
TLC : Rf 0.59 (hexane:ethyl acetate=1:1).

Example 1(106)

4-(N-phenylsulfamoyl)phenyl 2RS-(4-aminophenyl)butanoic acid ester

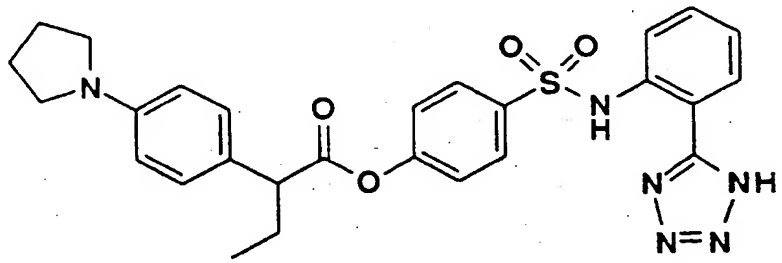


NMR ($DMSO-d_6$): δ 7.72 (2H, d, J=8Hz), 7.42-6.91 (9H, m), 6.80-6.54 (3H, m), 3.56 (1H, t, J=7Hz), 2.23-1.64

(2H, m), 0.92 (3H, t, J=7Hz);
TLC : Rf 0.39 (hexane:ethyl acetate=1:1).

Example 1(107)

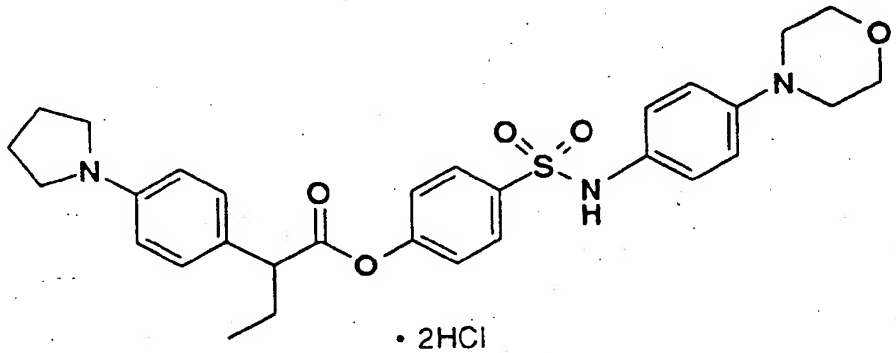
4-(N-(2-(tetrazol-5-yl)phenyl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.76 (1H, d, J=7.8Hz), 7.59 (1H, d, J=7.8Hz), 7.48 (1H, t-like), 7.35 (2H, d, J=8.8Hz), 7.26 (1H, t-like), 7.17 (2H, d, J=8.4Hz), 6.77 (2H, d, J=8.6Hz), 6.55 (2H, d, J=8.4Hz), 3.57 (1H, t, J=7.2Hz), 3.31-3.24 (4H, t-like), 2.25-1.75 (2H, m), 2.05-1.95 (4H, m), 0.97 (3H, t, J=7.2Hz);
TLC : Rf 0.33 (acetic acid:methanol:chloroform=1:20:200).

Example 1(108)

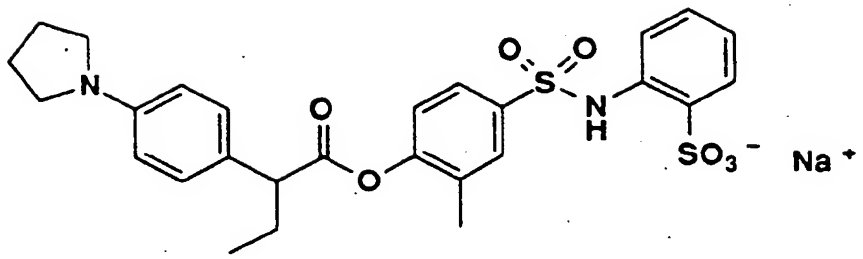
4-(N-4-(morpholin-4-yl)phenylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester 2hydrochloride



NMR (CD_3OD): δ 7.83 (2H, d, J=8.8Hz), 7.60 (4H, s), 7.55 (2H, d, J=9.0Hz), 7.29 (2H, d, J=9.0Hz), 7.16 (2H, d, J=8.8Hz), 4.05 (4H, t-like), 3.89 (1H, t, J=7.4Hz), 3.84-3.68 (4H, m), 3.58 (4H, t-like), 2.35-2.23 (4H, m), 2.30-2.09 and 2.04-1.78 (each 1H, m), 0.96 (3H, t, J=7.2Hz);
TLC : Rf 0.52 (methanol:chloroform=1:20).

Example 1(109)

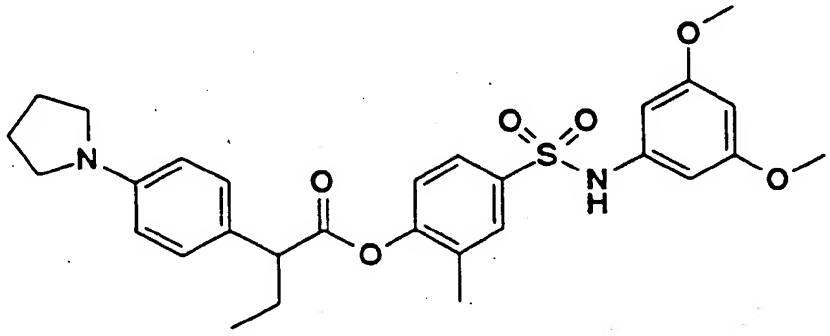
2-(N-(4-(2RS-(4-(pyrrolidin-1-yl)phenyl)butylyloxy)-3-methylphenyl sulfonyl)amino)phenylsulfonic acid sodium salt



NMR (DMSO-d_6): δ 10.6 (1H, s), 7.81 (1H, d, J=2Hz), 7.71 (1H, dd, J=9,2Hz), 7.57 (1H, dd, J=8,2Hz), 7.37 (1H, dd, J=8,1Hz), 7.22 (1H, td, J=8,1Hz), 7.16 (2H, d, J=9Hz), 7.06 (1H, d, J=9Hz), 6.97 (1H, td, J=8,1Hz), 6.57 (2H, d, J=9Hz), 3.67 (1H, t, J=7Hz), 3.30-3.15 (4H, m), 2.18-1.90 (5H, m), 1.88 (3H, s), 1.87-1.65 (1H, m), 0.86 (3H, t, J=7Hz);
TLC : Rf 0.19 (chloroform:methanol:acetic acid=25:5:1).

Example 1(110)

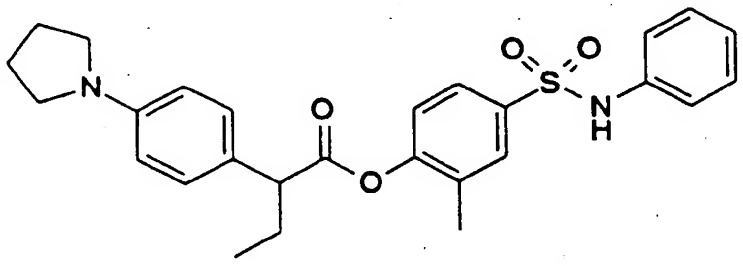
4-(N-3,5-dimethoxyphenylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.62-7.55 (2H, m), 7.18 (2H, d, J=8.4Hz), 6.98 (1H, d, J=8.2Hz), 6.69 (1H, s), 6.52 (2H, d, J=8.4Hz), 6.21-6.16 (3H, m), 3.69 (6H, s), 3.57 (1H, t, J=7.6Hz), 3.31-3.24 (4H, m), 2.25-1.80 (9H, m), 0.97 (3H, t, J=7.4Hz);
TLC : Rf 0.83 (hexane:ethyl acetate=1:1).

Example 1(111)

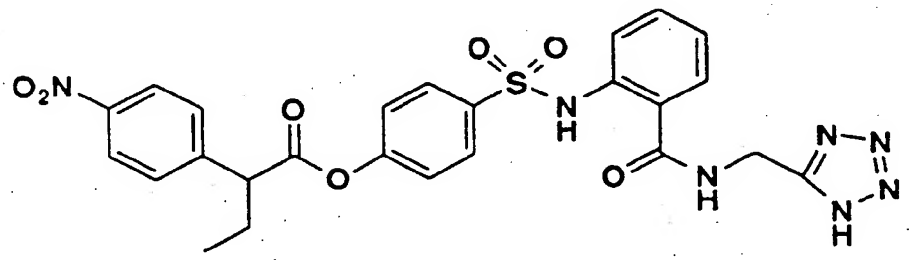
4-(N-phenylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.56-7.49 (2H, m), 7.26-6.94 (8H, m), 6.68 (1H, brs), 6.52 (2H, d, J=8.4Hz), 3.57 (1H, t, J=7.8Hz), 3.31-3.24 (4H, m), 2.27-1.75 (6H, m), 1.95 (3H, s), 0.97 (3H, t, J=7.4Hz);
TLC : Rf 0.83 (hexane:ethyl acetate=3:1).

Example 1(112)

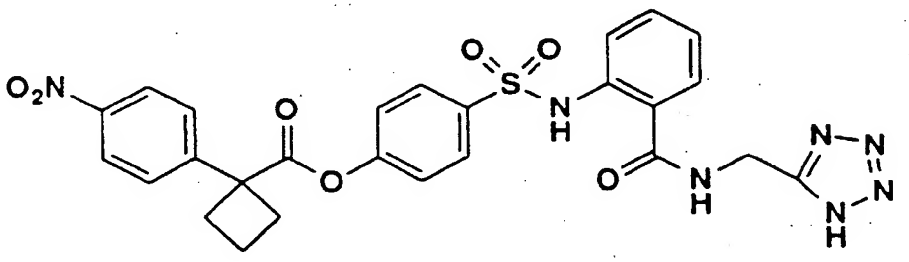
4-(N-2-(N'-(tetrazol-5-ylmethyl)carbamoyl)benzen-1-ylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 9.60-9.48 (1H, m), 8.25 (2H, d, J=8Hz), 7.88-7.63 (5H, m), 7.55-7.45 (2H, m), 7.30-7.09 (3H, m), 4.79-4.65 (2H, m), 4.13 (1H, t, J=7Hz), 2.31-2.04 (1H, m), 2.04-1.78 (1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.28 (acetic acid:methanol:chloroform=1:2:30).

Example 1(113)

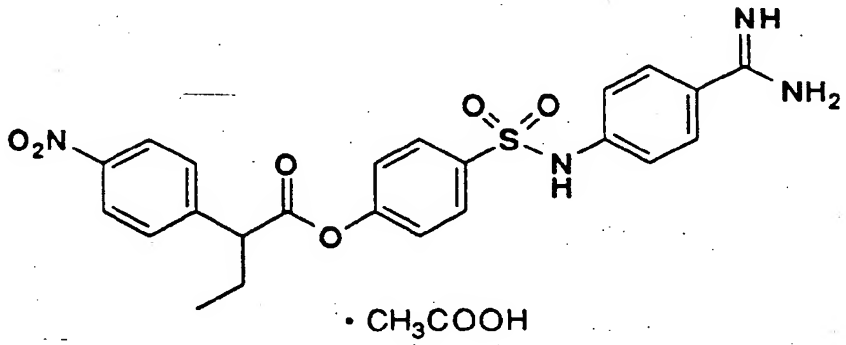
4-(N-2-(N'-(tetrazol-5-ylmethyl)carbamoyl)benzen-1-ylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.60-9.48 (1H, m), 8.33-8.20 (2H, m), 7.85-7.62 (5H, m), 7.55-7.40 (2H, m), 7.30-7.10 (3H, m), 4.78-4,65 (2H, m), 3.06-2.85 (2H, m), 2.75-2.55 (2H, m), 2.26-2.03 (1H, m), 2.03-1.80 (1H, m);
TLC : Rf 0.39 (acetic acid:methanol:chloroform=1:2:20).

Example 1(114)

4-(N-(4-amidinophenyl)sulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester · acetate

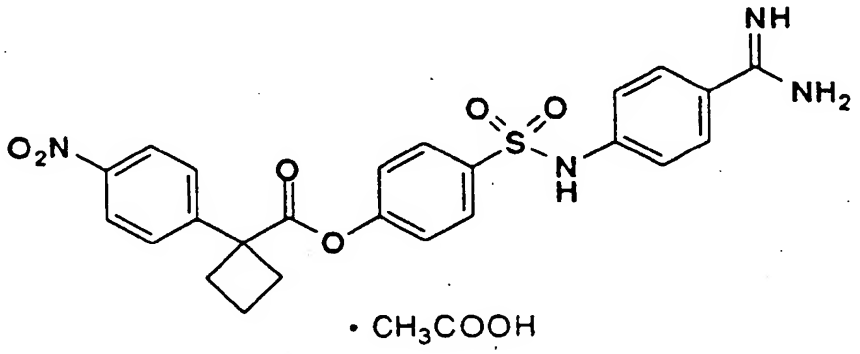


NMR (DMSO-d_6): δ 9.40-9.10 (2H, m), 8.75-8.55 (2H, m), 8.24 (2H, d, J=8Hz), 7.78-7.61 (4H, m), 7.44 (2H, d, J=8Hz), 7.05 (2H, d, J=8Hz), 6.83 (2H, d, J=8Hz), 4.09 (1H, t, J=7Hz), 2.23-2.00 (1H, m), 1.95-1.65 (4H, m), 0.88 (3H, t, J=7Hz);

TLC : Rf 0.52 (acetic acid:methanol:chloroform=1:2:10).

Example 1(115)

4-(N-(4-amidinophenyl)sulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester · acetate

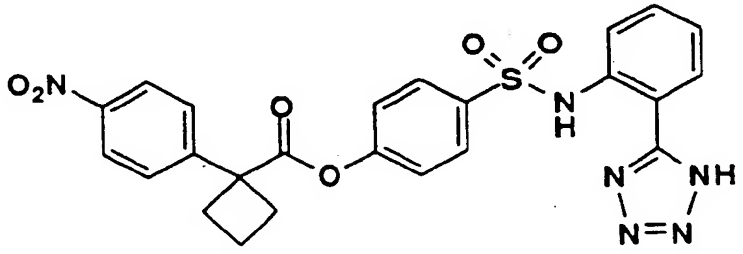


NMR (CD_3OD): δ 8.26 (2H, d, J=8Hz), 7.87 (2H, d, J=8Hz), 7.63 (4H, d, J=8Hz), 7.23 (2H, d, J=8Hz), 7.12 (2H, d, J=8Hz), 3.10-2.94 (2H, m), 2.78-2.60 (2H, m), 2.35-1.95 (5H, m);

TLC : Rf 0.40 (acetic acid:methanol:chloroform=1:2:15).

Example 1(116)

4-(N-2-(tetrazol-5-yl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester

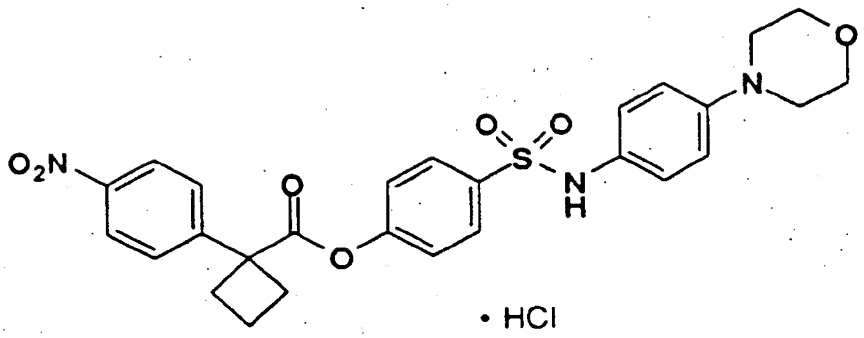


NMR (CD_3OD): δ 8.22 (2H, d, J=8.8Hz), 7.86-7.18 (8H, m), 6.96 (2H, d, J=8.8Hz), 3.08-2.88 (2H, m), 2.65 (2H, q-like), 2.28-2.08 (2H, m), 2.08-1.88 (2H, m);

TLC : Rf 0.43 (acetic acid:methanol:chloroform=1:3:30).

Example 1(117)

4-(N-4-(morpholin-4-yl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester · hydrochloride

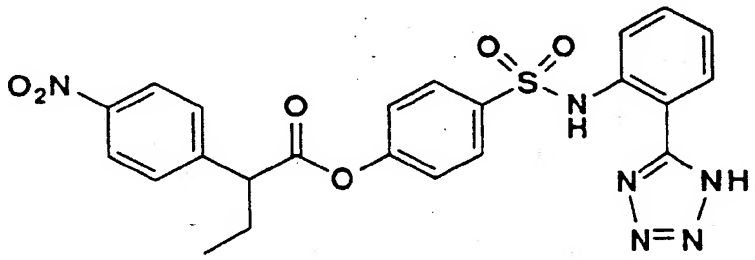


NMR (CD_3OD): δ 8.25 (2H, d, J=8.8Hz), 7.82 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.8Hz), 7.54 (2H, d, J=8.8Hz), 7 28 (2H, d, J=8.8Hz), 7.12 (2H, d, J=8.8Hz), 4.08 (4H, t, J=4.8Hz), 3.57 (4H, t, J=4.8Hz), 3.02 (2H, m), 2.70 (2H, m), 2 21 (1H, m), 2.03 (1H, m);

TLC : Rf 0.35 (hexane:ethyl acetate=1:1).

Example 1(118)

4-(N-2-(tetrazol-5-yl)phenylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester

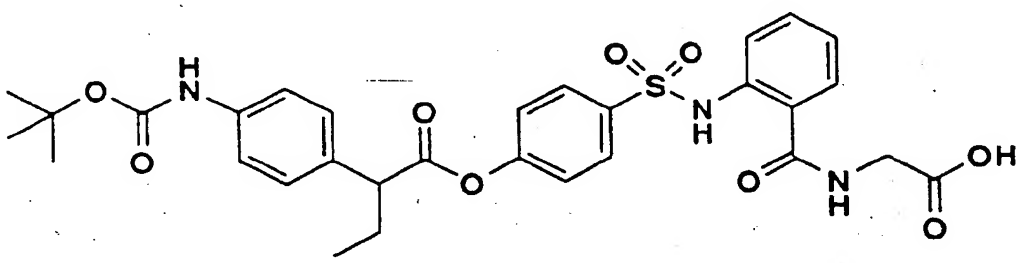


NMR (CD_3OD): δ 8.22 (2H, m), 7.93 (1H, d, J=7.8Hz), 7.68 (1H, d, J=7.8Hz), 7.64-7.60 (2H, t-like),7.60-7.56 (2H, m), 7.33 (1H, t, J=7.8Hz), 7.16 (1H, t, J=7.8Hz), 7.00-6.92 (2H, m), 3.92 (1H, t, J=8.0Hz), 2.30-2.05 and 2.05-1.75 (each 1H, m), 0.93 (3H, t, J=7.2Hz);

TLC : Rf 0.27 (acetic acid:methanol:chloroform=1:20:200).

Example 1(119)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-t-butyloxycarbonylamino)phenyl)butanoic acid ester

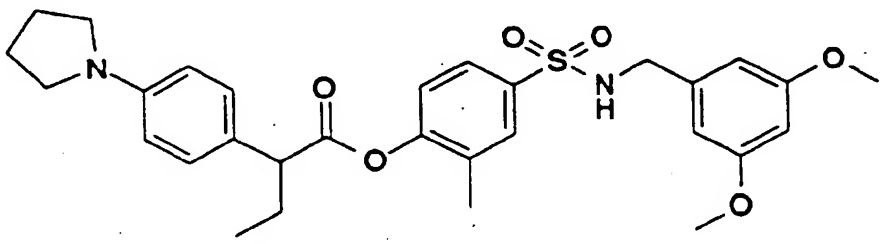


NMR ($DMSO-d_6$): δ 10.77 (1H, brs), 9.34 (1H, t-like), 7.82 (1H, d, J=7Hz), 7.79 (2H, d, J=8Hz), 7.44 (2H, d,

J=8Hz), 7.28-7.04 (7H, m), 6.78-6.70 (1H, m), 3.86 (2H, d-like), 3.72 (1H, t, J=7Hz), 2.11-1.90 and 1.81-1.67 (each 1H, m), 1.47 (9H, s), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.21 (chloroform:methanol:water=8:2:0.2).

Example 1(120)

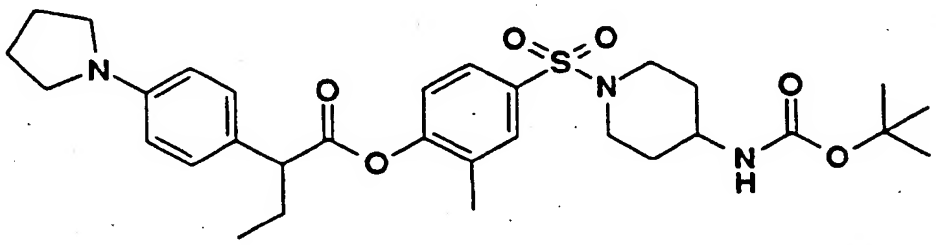
4-(3,5-dimethoxybenzylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.67-7.62 (2H, m), 7.22 (2H, d, J=8.6Hz), 7.05 (1H, d, J=9.4Hz), 6.54 (2H, d, J=8.6Hz), 6.32 (3H, s), 4.64 (1H, t, J=6.0Hz), 4.05 (2H, d, J=6.0Hz), 3.72 (6H, s), 3.61 (1H, t, J=7.6Hz), 3.33-3.26 (4H, m), 2.27-1.81 (6H, m), 2.02 (3H, s), 0.99 (3H, t, J=7.2Hz);
TLC : Rf 0.86 (hexane:ethyl acetate=1:1).

Example 1(121)

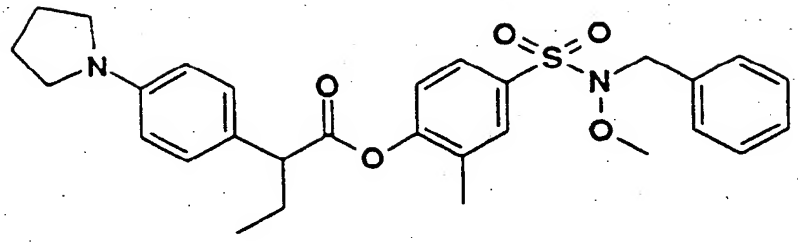
4-((4-t-butoxycarbonylaminopiperidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.55 (1H, s), 7.53 (1H, d, J=8.4Hz), 7.23 (2H, d, J=8.6Hz),7.08 (1H, d, J=8.4Hz), 6.55 (2H, d, J=8.6Hz), 4.40 (1H, brs), 3.7-3.6 (2H, br), 3.62 (1H, t, J=7.7Hz), 3.5-3.2 (1H, br), 3.28 (4H, br), 2.6-2.4 (2H, m), 2.3-2.1 (1H, m), 2.04 (3H, s), 2.00 (4H, brs), 2.1-1.8 (1H, m), 1.6-1.4 (4H, m), 1.41 (9H, s), 0.99 (3H, t, J=7.3Hz);
TLC : Rf 0.81 (hexane:ethyl acetate=1 :1).

Example 1(122)

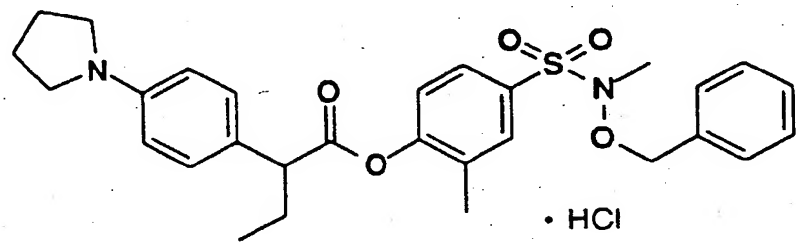
4-(N-methoxy-N-benzylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.74 (1H, s), 7.72 (1H, d, J=9.0Hz), 7.32 (5H, s), 7.24 (2H, d, J=8.8Hz), 7.14 (1H, d, J=9.0Hz), 6.56 (2H, d, J=8.8Hz), 3.98 (2H, s), 3.64 (1H, t, J=7.7Hz), 3.43 (3H, s), 3.29 (4H, brs), 2.3-2.1 (1H, m), 2.08 (3H, s), 2.00 (4H, brs), 2.1-1.8 (1H, m), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.79 (hexane:ethyl acetate=2:1).

Example 1(123)

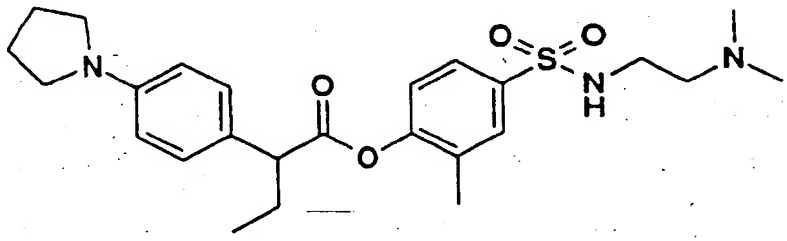
4-(N-benzyloxy-N-methylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ7.71 (1H, s), 7.68 (1H, d, J=8.2Hz), 7.5-7.2 (9H, brs), 7.09 (1H, d, J=8.2Hz), 5.00 (2H, s), 3.73 (1H, t, J=7,5Hz), 3.7-3.4 (4H, m), 2.65 (3H, s), 2.4-2.1 (5H, m), 2.03 (3H, s), 2.1-1.8 (1H, m), 0.99 (3H, t, J=7.2Hz);
TLC : Rf 0.66 (hexane:ethyl acetate=2:1).

Example 1(124)

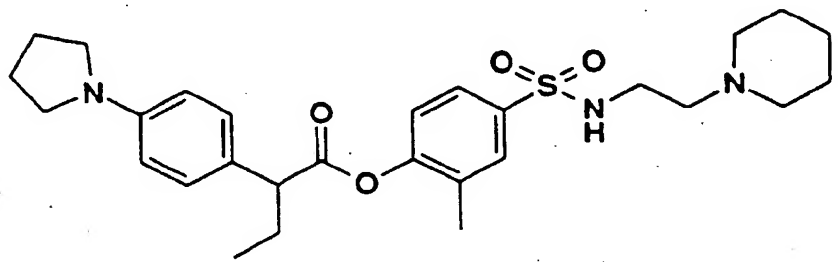
4-(2-(N,N-dimethylamino)ethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.69-7.63 (2H, m), 7.22 (2H, d, J=8.6Hz), 7.05 (1H, d, J=8.4Hz), 6.55 (2H, d, J=8.6Hz), 3.61 (1H, t, J=8.2Hz), 3.32-3.25 (4H, m), 2.95 (2H, t, J=5.8Hz), 2.30 (2H, t, J=5.8Hz), 2.27-1.65 (15H, m), 0.99 (3H, t, J=7.2Hz);
TLC : Rf 0.72 (chloroform:methanol:water=8:2:0.2).

Example 1(125)

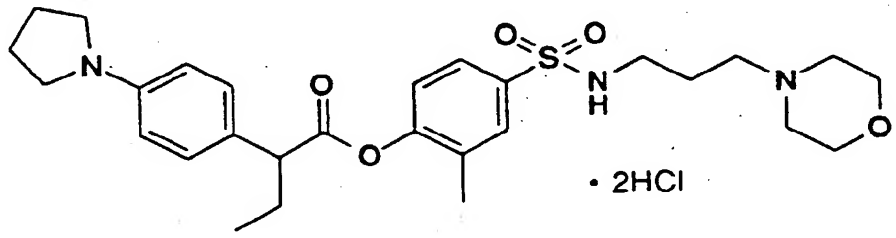
4-(2-(piperidin-1-yl)ethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.7-7.4 (m, 2H), 7.23 (d, J=8.7Hz, 2H), 7.05 (d, J=8.4Hz, 1H), 6.56 (d, J=8.7Hz, 2H), 3.61 (t, J=7.4Hz, 1H), 3.4-3.2 (m, 4H), 3.1-2.9 (m 2H), 2.5-2.4 (m, 2H), 2,4-2.3 (m, 4H), 2.3-1.8 (m, 2H), 2.1-1.9 (m, 4H), 2.03 (s, 3H), 1.6-1.3 (m, 6H), 0.99 (t, J=7.4Hz, 3H);
TLC : Rf 0.55 (chloroform:methanol=7:1).

Example 1(126)

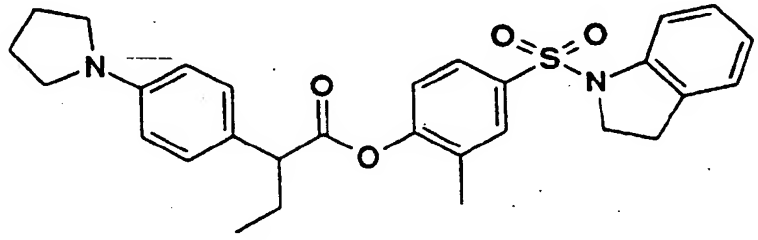
4-(3-(morpholin-4-yl)propylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR ($CDCl_3$): δ7.8-7.4 (m, 5H), 7.3-7.0 (m, 3H), 4.3-3.4 (m, 11H), 3.2-2.8 (m, 6H), 2.4-1.8 (m, 11H), 0.99 (t, J=7.2Hz, 3H);
TLC : Rf 0.56 (chloroform:methanol=9:1).

Example 1(127)

4-(indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

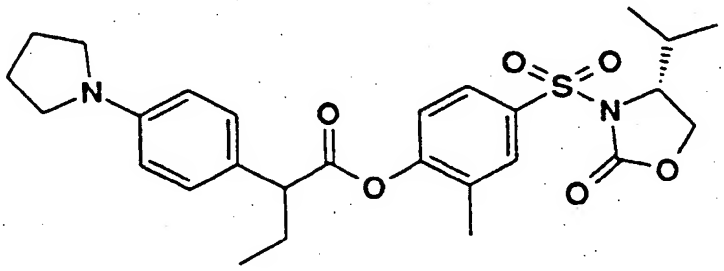


NMR ($CDCl_3$): δ7.66-7.51 (3H, m), 7.24-6.88 (6H, m), 6.53 (2H, d, J=8.8Hz), 3.88 (2H, t, J=8.4Hz), 3.58 (1H, t, J=7.8Hz), 3.27 (4H, m), 2.89 (2H, t, J=8.4Hz), 2.29-1.72 (9H, m), 0.96 (3H, t, J=7.2Hz);

TLC : Rf 0.80 (hexane:ethyl acetate=1:1).

Example 1(128)

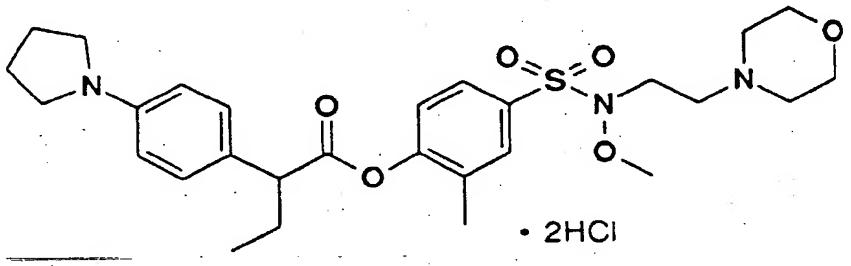
4-((2-oxo-4R-isopropylperhydroxazol-3-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ7.93 (1H, s), 7.86 (1H, d, J=8.6Hz), 7.22 (2H, d, J=8.4Hz), 7.11 (1H, d, J=8.6Hz), 6.55 (2H, d, J=8.4Hz), 4.43-4.33 (1H, m), 4.26 (1H, t, J=8.6Hz), 4.15 (1H, dd, J=8.6, 3.2Hz), 3.61 (1H, t, J=7.7Hz), 3.40-3.20 (4H, m), 2.55-2.33 (1H, m), 2.33-1.70 (9H, m), 0.99 (3H, t, J=7.4Hz), 0.91 (3H, d, J=6.9Hz), 0.76 (3H, d, J=6.9Hz);
TLC : Rf 0.43 (hexane:ethyl acetate=7:3).

Example 1(129)

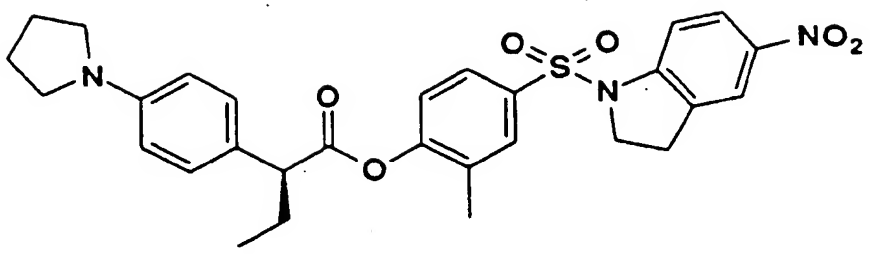
4-(N-2-(morpholin-4-yl)ethyl-N-methoxyaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2 hydrochloride



NMR ($DMSO-d_6$): δ7.85-7.65 (2H, m), 7.27 (3H, d, J=8.0Hz), 6.95-6.70 (2H, brd), 4.05-3.70 (5H, m), 3.85 (3H, s), 3.50-2.95 (12H, m), 2.30-1.65 (6H, m), 2.02 (3H, s), 0.92 (3H, t, J=7.5Hz);
TLC : Rf 0.52 (hexane:ethyl acetate=2:1).

Example 1(130)

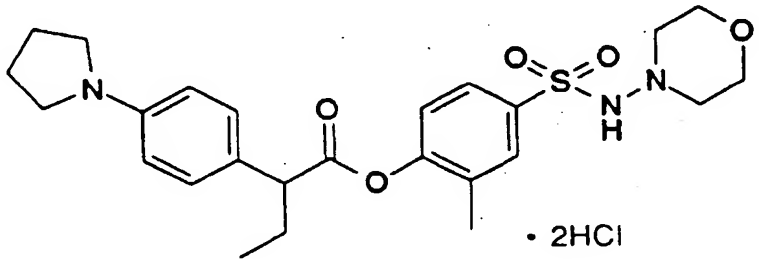
4-(5-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ8.10 (1H, d, J= 9.0Hz), 7.95 (1H, s), 7.72-7.56 (3H, m), 7.18 (2H, d, J=8.0Hz), 7.05 (1H, d, J=8.0Hz), 6.52 (2H, d, J=8.0Hz), 4.01 (2H, t, J=8.5Hz), 3.58 (1H, t, J=7.5Hz), 3.35-3.18 (4H, m), 3.08 (2H, t, J=8.5Hz), 2.30-1.70 (6H, m), 2.00 (3H, s), 0.96 (3H, t, J=7.5Hz);
TLC : Rf 0.60 (hexane:ethyl acetate=2:1).

Example 1(131)

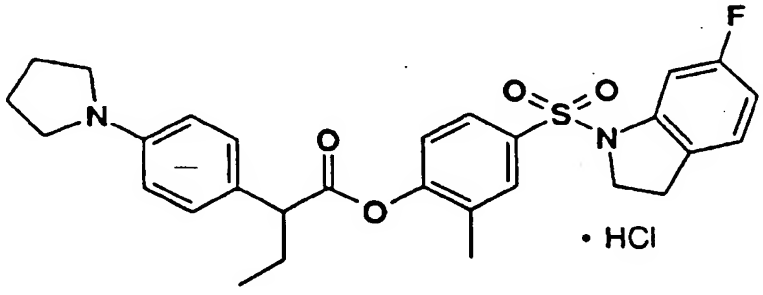
4-(morpholin-4-ylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (CD_3OD): δ7.84-7.70 (2H, m), 7.64 (4H, s-like), 7.13 (1H, d, J=8.2Hz), 3.97 (1H, t, J=7.4Hz), 3.87-3.66 (4H, m), 3.54 (4H, t, J=4.4Hz), 2.55 (4H, t, J=4.4Hz), 2.43-2.14 (5H, m), 2.14-1.80 (4H, m), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.51 (hexane:ethyl acetate=1:1).

Example 1(132)

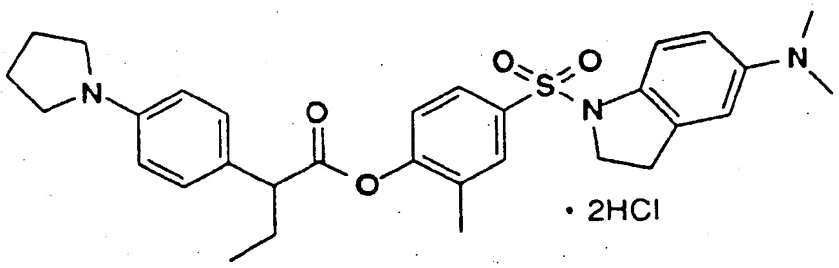
4-(6-fluoroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD:$CDCl_3$=1:1): δ7.75-7.40 (6H, m), 7.29 (1H, dd, J=10.0 and 2.0Hz), 7.15-7.01 (2H, m), 6.69 (1H, td, J=8.6 and 2.0Hz), 3.94 (2H, t, J=8.4Hz), 3.87 (1H, t, J=7.6Hz), 3.79-3.63 (4H, m), 2.89 (2H, t, J=8.4Hz), 2.40-2.12 (5H, m), 2.08-1.79 (4H, m), 0.99 (3H, t, J=7.4Hz);
TLC : Rf 0.29 (hexane :ethyl acetate=3:1).

Example 1(133)

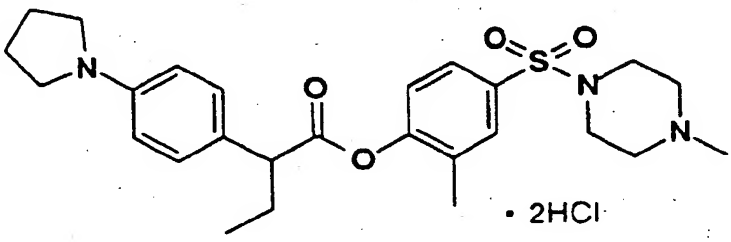
4-(5-(N,N-dimethylamino)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2 hydrochloride



NMR (CD_3OD): δ7.78-7.64 (3H, m), 7.60 (4H, s-like), 7.52-7.42 (2H, m), 7.11 (1H, d, J=8.4Hz), 4.01 (2H, t, J=8.5Hz), 3.93 (1H, t, J=8.4Hz), 3.87-3.70 (4H, m), 3.23 (6H, s), 3.06 (2H, t, J=8.5Hz), 2.40-2.10 (5H, m), 2.10-1.80 (4H, m), 0.97 (3H, t, J=7.2Hz);
TLC : Rf 0.24 (hexane :ethyl acetate=3:1).

Example 1(134)

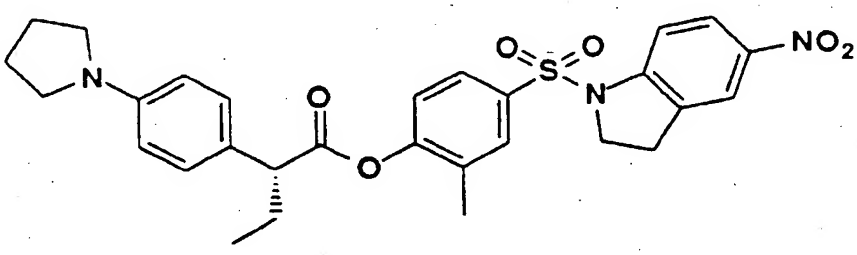
4-(4-methylpiperazin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2 hydrochloride



NMR (CD_3OD): δ7.75-7.59 (6H, m), 7.23 (1H, d, J=8.2Hz), 4.06-3.84 (3H, m), 3.84-3.68 (4H, m), 3.64-3.49 (2H, m), 3.32-3.11 (2H, m), 2.89 (3H, s), 2.84-2.64 (2H, m), 2.44-2.14 (5H, m), 2.13-1.82 (4H, m), 1.00 (3H, t, J=7.2Hz);
TLC : Rf 0.36 (ethyl acetate).

Example 1(135)

4-(5-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



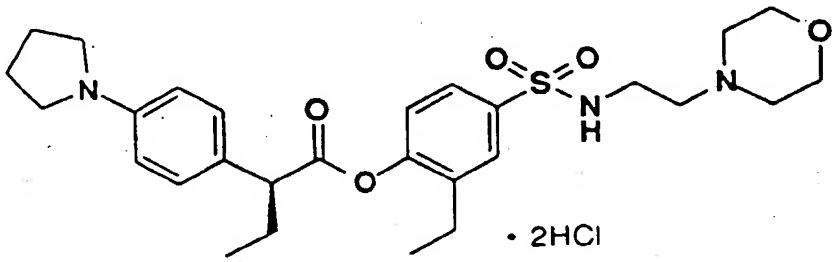
NMR ($CDCl_3$): δ8.10 (1H, dd, J=9.0, 2.2Hz), 7.95 (1H, d, J=2.2Hz), 7.66 (1H, d, J=9.0HZ), 7.66 (1H, s), 7.63 (1H,

d, J=8.2Hz), 7.18 (2H, d, J=8.8Hz), 7.05 (1H, d, J=8.2Hz), 6.53 (2H, d, J=8.8Hz), 4.01 (2H, t, J=8.5Hz), 3.58 (1H, t, J=7.7Hz), 3.3-3.2 (4H, brs), 3.08 (2H, t, J=8.5Hz), 2.3-2.0 (1H, m), 2.1-1.9 (4H, brs), 2.00 (3H, s), 2.0-1.8 (1H, m), 0.96 (3H, t, J=7.3Hz);

TLC : Rf 0.60 (hexane:ethyl acetate=2:1).

Example 1(136)

4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-ethylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

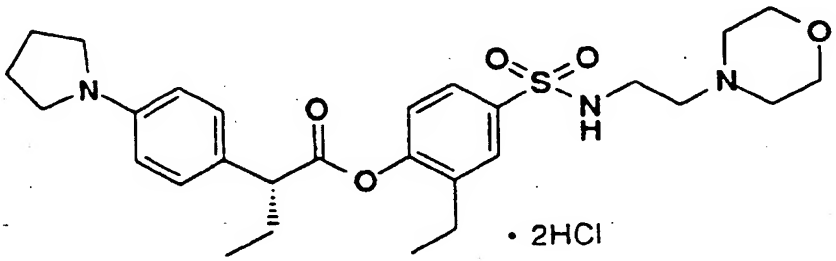


NMR (CD_3OD): δ7.83-7.58 (6H, m), 7.18 (1H, d, J=8.0Hz), 4.12-3.70 (9H, m), 3.53 (2H, d, J=12.0Hz), 3.38-3.08 (6H, m), 2.45-1.80 (8H, m), 1.00 (6H, t, J=7.5Hz);

TLC : Rf 0.41 (hexane:ethyl acetate=1:4).

Example 1(137)

4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-ethylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

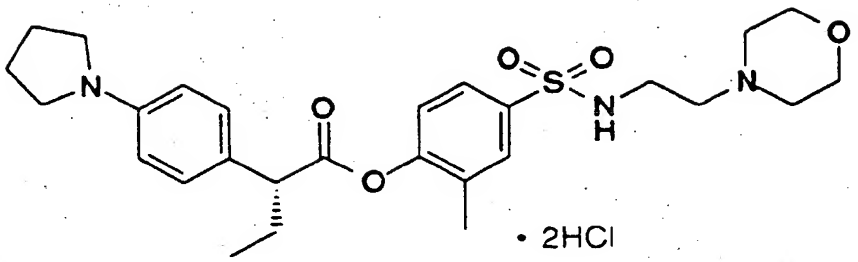


NMR (CD_3OD): δ7.83-7.58 (6H, m), 7.19 (1H, d, J=8.0Hz), 4.12-3.70 (9H, m), 3.53 (2H, d, J=12.0Hz), 3.40-3.08 (6H, m), 2.50-1.80 (8H, m), 0.99 (6H, t, J=7.5Hz);

TLC : Rf 0.41 (hexane:ethyl acetate=1:4).

Example 1(138)

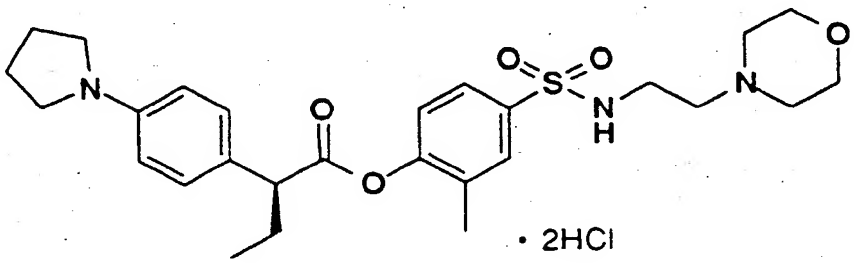
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (DMSO-d_6): δ11.0-10.8 (1H, brs), 7.75 (1H, s), 7.70 (1H, d, J=8.6Hz), 7.22 (2H, d, J=8.4Hz), 7.18 (1H, d, J=8.6Hz), 6.64 (2H, d, J=8.4Hz), 4.0-3.7 (5H, m), 3.4-3.0 (12H, m), 2.2-2.0 (1H, m), 2.1-1.9 (4H, brs), 2.0-1.7 (1H, m), 1.97 (3H, s), 0.91 (3H, t, J=7.3Hz);
TLC : Rf 0.50 (chloroform:methanol=9:1).

Example 1(139)

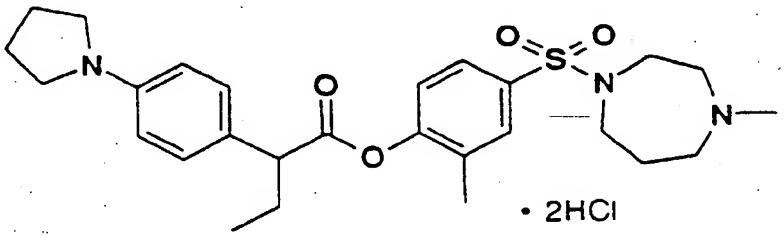
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (DMSO-d_6): δ11.4-11.2 (1H, brs), 7.76 (1H, s), 7.70 (1H, d, J=8.6Hz), 7.30 (2H, d, J=8.4Hz), 7.18 (1H, d, J=8.6Hz), 6.87 (2H, d, J=8.4Hz), 4.0-3.7 (5H, m), 3.5-3.3 (6H, m), 3.3-3.0 (6H, m), 2.2-2.0 (1H, m), 2.1-1.9 (4H, brs), 2.0-1.7 (1H, m), 1.98 (3H, s), 0.91 (3H, t, J=7.2Hz);
TLC : Rf 0.50 (chloroform:methanol=9:1).

Example 1(140)

4-(4-methyl-1 ,4-perhydrodiazepin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

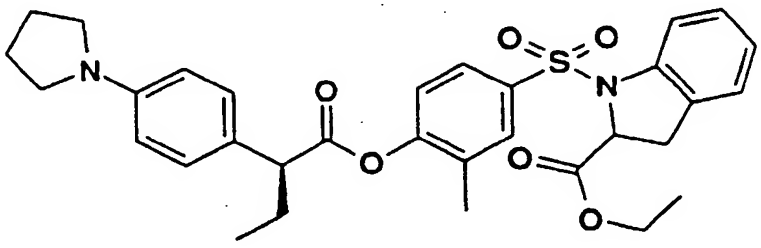


NMR (DMSO-d_6): δ7.72 (1H, d, J=2Hz), 7.66 (1H, dd, J=2 and 8Hz), 7.25 (2H, d, J=8Hz), 7.19 (1H, d, J=8Hz), 6.76 (2H, d-like), 3.76 (1H, t, J=7Hz), 3.75-3.01 (12H, m), 2.76 and 2.74 (total 3H, each s), 2.21-1.66 (8H, m), 1.99 (3H, s), 0.91 (3H, t, J=7Hz);

TLC : Rf 0.52 (chloroform:methanol:water=9:1:0.1).

Example 1(141)

4-(2RS-ethoxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

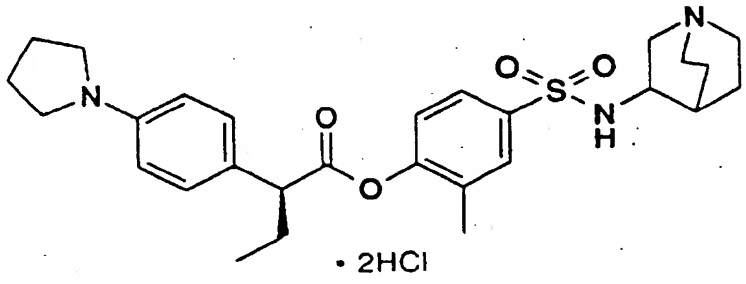


NMR ($CDCl_3$): δ7.62-7.51 (3H, m), 7.23-7.15 (3H, m), 7.07-6.95 (3H, m), 6.52 (2H, d, J=9Hz), 4.75-4.67 (1H, m), 4.24 (2H, q, J=7Hz), 3.57 (1H, t, J=7Hz), 3.31-3.24 (4H, m), 3.21-3.00 (2H, m), 2.23-1.75 (2H, m), 2.04-1.99 (4H, m), 1.96 (3H, s), 1.29 (3H, t, J=7Hz), 0.96 (3H, t, J=7Hz);

TLC : Rf 0.29 (hexane:ethyl acetate=3:1).

Example 1(142)

4-(quinudidin-3RS-ylaminosulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

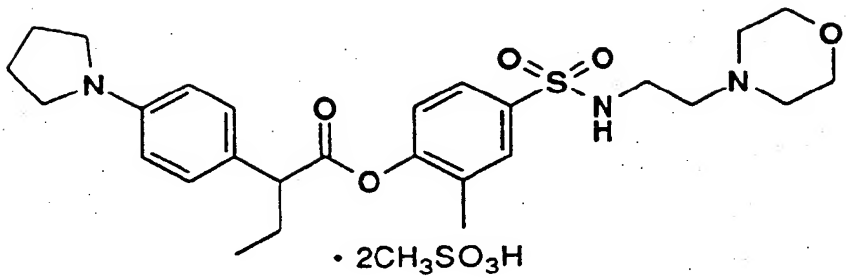


NMR (DMSO-d_6): δ8.35 (1H, d, J=7Hz), 7.74-7.64 (2H, m), 7.26 (2H, d, J=8Hz), 7.17 (1H, d, J=8Hz), 6.82-6.70 (2H, br), 3.75 (1H, t, J=7Hz), 3.61-3.43 (1H, br), 3.40-3.22 (5H, m), 3.18-2.94 (5H, m), 2.90-2.79 (1H, m), 2.17-1.60 (13H, m), 0.91 (3H, t, J=7Hz);

TLC : Rf 0.35 (chloroform:methanol:water=8:2:0.2).

Example 1(143)

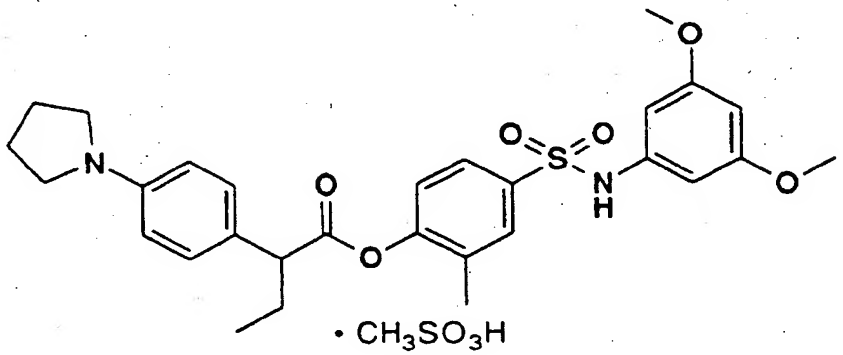
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2methanesulfonic acid salt



NMR (CD_3OD): δ7.80-7.70 (2H, m), 7.67 (4H, s), 7.17 (1 H, d, J=8.0Hz), 4.10-3.70 (9H, m), 3.54 (2H, d, J=12.0Hz), 3.40-3.10 (6H, m), 2.70 (6H, s), 2.40-1.80 (6H, m), 2.05 (3H, s), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.31 (chloroform:methanol:acetic acid=40:2:1).

Example 1(144)

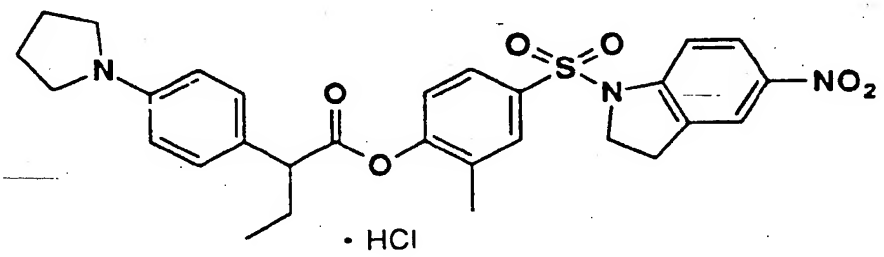
4-(3,5-dimethoxyphenylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · methanesulfonic acid salt



NMR (CD_3OD): δ7.70-7.50 (6H, m), 7.05 (1H, d, J=8.5Hz), 6.24 (2H, d, J=2.0Hz), 6.16 (1H, t, J=2.0Hz), 3.94 (1H, t, J=7.5Hz), 3.77 (4H, t-like), 3.67 (6H, s), 2.70 (3H, s), 2.40-1.80 (6H, m), 1.96 (3H, s), 0.98 (3H, t, J=7.5Hz);
TLC : Rt 0.73 (hexane:ethyl acetate=1:1).

Example 1(145)

4-(5-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

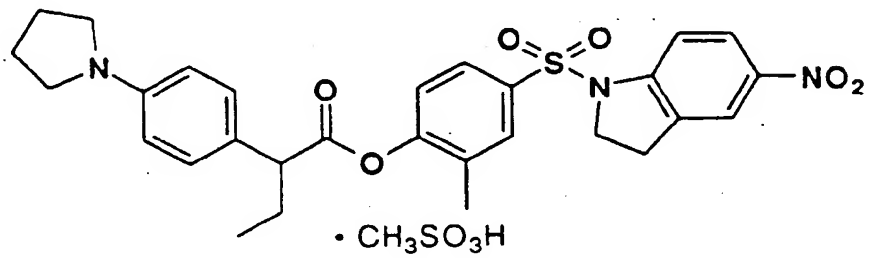


NMR ($CDCl_3$): δ8.11 (1H, dd, J=2.0, 9.0Hz), 7.96 (1H, d, J=2.0Hz), 7.72-7.60 (3H, m), 7.55 (2H, d, J=8.0Hz), 7.44 (2H, d, J=8.0Hz), 7.06 (1H, d, J=8.0Hz), 4.03 (2H, t, J=8.5Hz), 3.75 (1H, t, J=7.5Hz), 3.85-3.40 (4H, m), 3.10 (2H,

t, J=8.5Hz), 2.45-2.20 (4H, m), 2.40-1.75 (2H, m), 2.02 (3H, s), 0.98 (3H, t, J=7.5Hz);
TLC : Rf 0.60 (hexane:ethyl acetate=2:1).

Example 1(146)

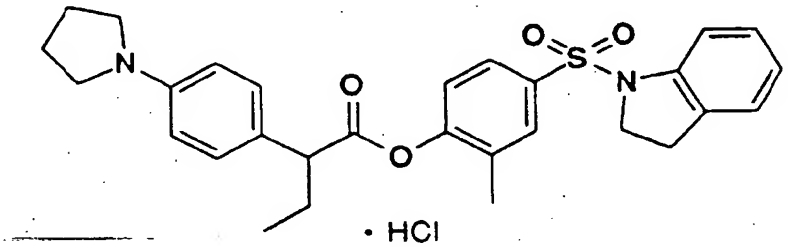
4-(5-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · methanesulfonic acid salt



NMR ($CDCl_3$): δ8.11 (1H, dd, J=2.5, 9.0Hz), 7.97 (1H, d, J=2.5Hz), 7.74-7.62 (3H, m), 7.57 (2H, d, J=8.5Hz), 7.49 (2H, d, J=8.5Hz), 7.07 (1H, d, J=8.0Hz), 4.03 (2H, t, J=8.5Hz), 3.77 (1H, t, J=7.5Hz), 4.10-3.30 (4H, m), 3.11 (2H, t, J=8.5Hz) 2.85 (3H, s), 2.50-2.20 (4H, m), 2.40-2.10 and 2.10-1.80 (each 1H, m), 2.04 (3H, s), 0.99 (3H, t, J=7.5Hz);
TLC : Rf 0.60 (hexane:ethyl acetate=2:1).

Example 1(147)

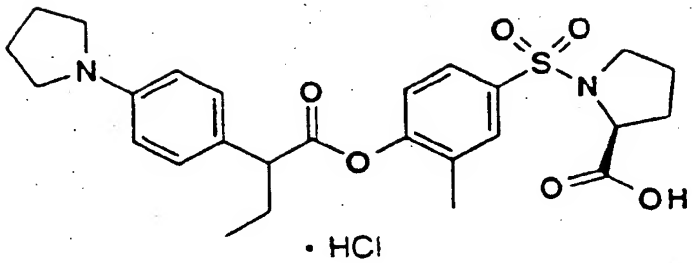
4-(indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ7.65-7.53 (3H, m), 7.32 (2H, d, J=8.4Hz), 7.24-6.90 (6H, m), 3.89 (2H, t, J=8.5Hz), 3.66 (1H, t, J=8.2Hz), 3.45 (4H, brs), 2.89 (2H, t, J=8.5Hz), 2.34-2.04 (5H, m), 1.97 (3H, s), 2.04-1.73 (1H, m), 0.97 (3H, t, J=7.2Hz);
TLC : Rf 0.42 (hexane:ethyl acetate=3:1).

Example 2

4-(2S-carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



• HCl

To a mixture solution of the compound prepared in example 1 (1.04 g) in dichloromethane(5 ml) and anisole (5 ml) were slowly added trifluoroacetic acid (5 ml) at 0 °C. The reaction mixture was stirred for 6h at room temperature. The reaction mixture was concentrated, and the residue was purified by column chromatography on silica gel (chloroform: methanol=20:1) to give N-{4-[2RS-(4-(1-pyrrolidinyl)phenyl)butylyloxy]-3-methylphenyl sulfonyl}-L-proline. The obtained above compound was converted to hydrochloride salt by the following method. To a solution of N-{4-[2RS-(4-(1-pyrrolidinyl)phenyl)butylyloxy]-3-methylphenyl sulfonyl}-L-proline in dioxane (5 ml) was added 4N hydrochloric acid in dioxane solution (1 ml) at 0 °C. The reaction mixture was stirred for 5 min, and reaction mixture was concentrated to give the title compound (1 g) having the following physical data.

NMR ($CDCl_3$): δ 7.70 (1H, s), 7.67 (1H, d, J=8.0Hz), 7.59 (2H, d, J=8.5Hz), 7.49 (2H, d, J=8.5Hz), 7.07 (1H, d, J=8.0Hz), 4.26 (1H, dd, J=3.5, 7.0Hz), 3.78 (1H, t, J=7.5Hz), 3.75-3.60 (4H, m), 3.52-3.40 (1H, m), 3.33-3.14 (1H, m), 2.40-2.25 (4H, m), 2.40-1.65 (6H, m), 2.04 (3H, s), 1.00 (3H, t, J=7.5Hz);

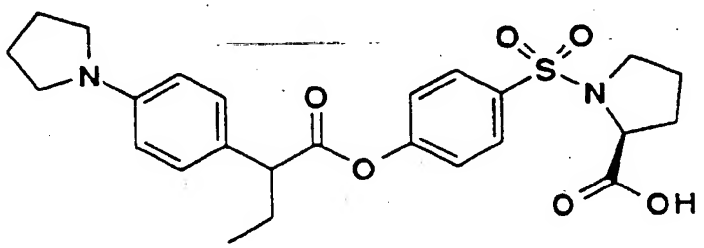
TLC : Rf 0.39 (acetic acid:methanol:chloroform=1:2:40).

Example 2(1)~2(296)

By the same procedure as example 1 and example 2 and by known method converted to corresponding salts, acid addition salts or solvates, the compounds having the following physical data were given by using corresponding phenol derivatives instead of the compound prepared in reference example 4 and by using corresponding carboxylic acid derivatives instead of the compound prepared in reference example 7.

Example 2(1)

4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



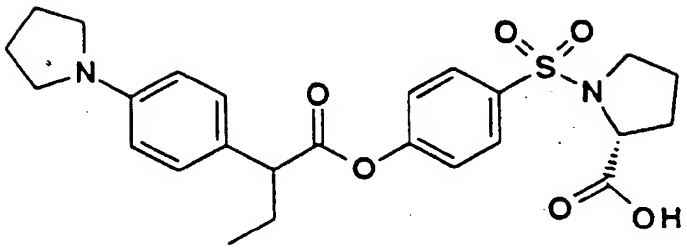
• HCl

NMR(DMSO-d_6): δ7.86 (2H, d, J=8Hz), 7.24 (4H, d, J=8Hz), 6.78 (2H, d, J=8Hz), 4 15-4.05 (1H, ml, 3.73 (1H, t, J=7Hz), 3.40-3.05 (6H, m),. 2.20-1.45 (10H, m), 0.89 (3H, t, J=7Hz);

TLC : Rf 0.26 (acetic acid:methanol:chloroform=1:2:60).

Example 2(2)

4-(2R-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

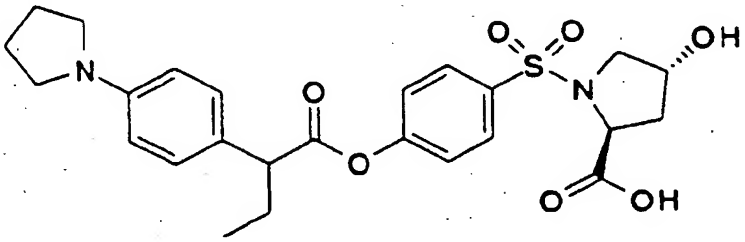


• HCl

NMR (DMSO-d_6): δ7.86 (2H, d, J=8.8Hz), 7.25 (4H, d, J=8.8Hz), 6.78 (2H, d, J=8.8Hz), 4.16-4.05 (1H, m), 3.74 (1H, t, J=7.2Hz), 3.44-3.06 (2H, m), 3.36-3.24 (4H, m), 2.22-1.46 (10H, m), 0.90 (3H, t, J=7.2Hz);
TLC : Rf 0.39 (acetic acid:methanol:chloroform=1:2:40).

Example 2(3)

4-(2S-carboxy-4R-hydroxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

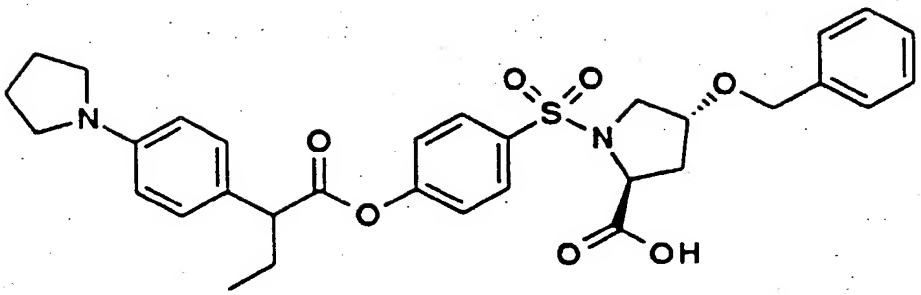


• HCl

NMR (DMSO-d_6): δ 7.83 (2H, d, J=9Hz), 7.31-7.18 (4H, m), 6.85-6.68 (2H. m), 4.25-4.14 (1H, m), 4.04 (1H, t, J=7Hz), 3.73 (1H, t, J=7Hz), 3.50-3.38 (5H, m). 3.18-3.05 (1H, m), 2.20-1.65 (8H, m), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.27 (chloroform:methanol:acetic acid=20:2:1).

Example 2(4)

4-(2S-carboxy-4R-benzyloxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



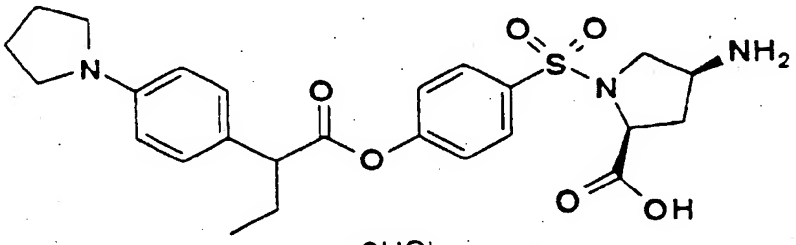
• HCl

NMR ($CDCl_3$): δ 7.84 (2H, d, J=9Hz), 7.62 (2H, d, J=9Hz), 7.47 (2H, d, J=9Hz), 7.34-7.19 (3H, m), 7.17-7.00 (4H, m), 4.30 (1H, t, J=8Hz), 4.23 (2H, s), 4.15-4.03 (1H, m), 3.86-3.42 (7H, m), 2.47-2.05 (7H, m), 2.05-1.74 (1H, m), 0.97 (3H, t, J=7Hz);

TLC : Rf 0.35 (chloroform:methanol:acetic acid=40:2:1).

Example 2(5)

4-(2S-carboxy-4S-aminopyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



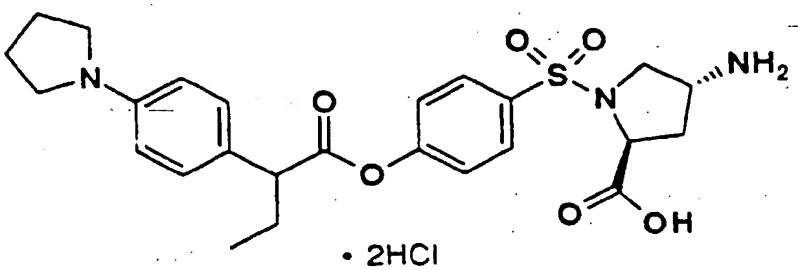
• 2HCl

NMR ($DMSO-d_6$): δ 8.55-8.20 (2H, brs), 7.89 (2H, d, J=9Hz), 7.29 (2H, d, J=9Hz), 7.25 (2H, d, J=9Hz), 6.73 (2H, d, J=9Hz), 5.80-4.40 (1H, m), 4.18 (1H, t, J=7Hz), 3.74 (1H, t, J=7Hz), 3.64-3.10 (7H, m), 2.67-2.40 (1H, m), 2.20-1.65 (7H, m), 0.90 (3H, t, J=7Hz);

TLC : Rf 0.49 (ethyl acetate:acetic acid:water=6:2:1).

Example 2(6)

4-(2S-carboxy-4R-aminopyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



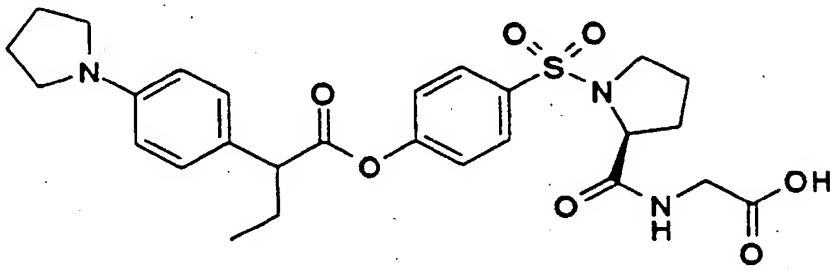
• 2HCl

NMR (DMSO-d_6): δ 8.60-8.30 (2H, brs), 7.88 (2H, d, J=9Hz), 7.28 (2H, d, J=9Hz), 7.23 (2H, d, J=9Hz), 6.72 (2H, d, J=9Hz), 5.40-4.20 (1H, m), 4.40 (1H, dd, J=9Hz, 4Hz), 3.90-3.50 (2H, m), 3.50-3.10 (6H, m), 2.33-1.60 (8H, m), 0.90 (3H, t, J=7Hz);

TLC : Rf 0.42 (ethyl acetate:acetic acid:water=6:2:1).

Example 2(7)

4-(2S-(N-carboxymethylcarbamoyl)pyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

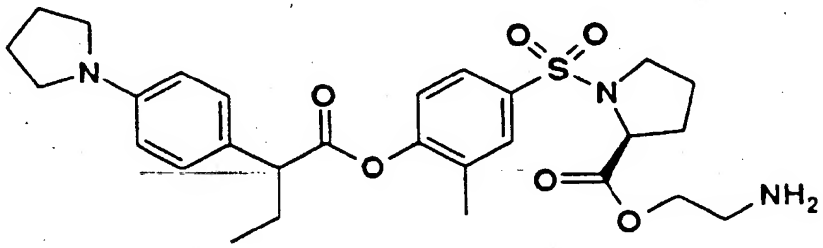


NMR ($CDCl_3$+CD_3OD): δ7.84 (2H, d, J=8.8Hz), 7.28-7.18 (4H, m), 6.72 (2H, d, J=8.8Hz), 4.09-3.85 (3H, m), 3.71-3.53 (2H, m), 3.41-3.31 (4H, m), 3.20-3.08 (1H, m), 2.26-1.59 (10H, m), 0.99 (3H, t, J=7.4Hz);

TLC : Rf 0.24 (chloroform:methanol:acetic acid=40:2:1).

Example 2(8)

4-(2S-(2-aminoethoxycarbonyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



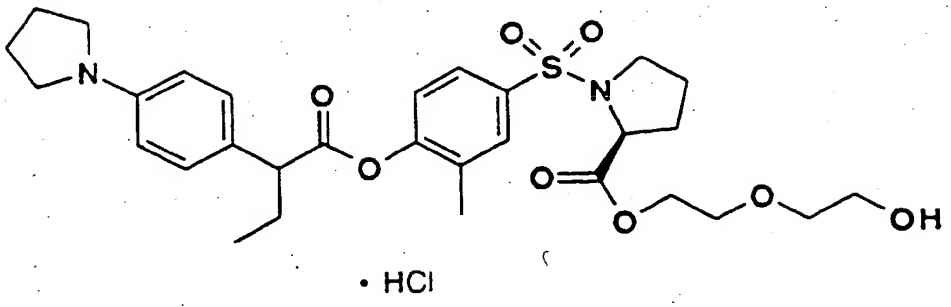
• 2HCl

NMR (DMSO-d_6): δ 8.21 (2H, brs), 7.75 (1H, s), 7.69 (1H, d, J=8.2Hz), 7.22 (3H, m), 6.70 (2H, d, J=8.8Hz), 4.26 (3H, m), 3.50-3.36 (2H, m), 3.31 (4H, m), 3.20 (1H, m), 3.08 (2H, m), 2.12 (1H, m), 2.00 (3H, s), 1.96 (4H, m), 1.87 (4H, m), 1,66 (1H, m), 0.92 (3H, t, J=7.2Hz);

TLC : Rf 0.31 (chloroform:methanol:acetic acid=12:1:1).

Example 2(9)

4-(2S-(2-(2-hydroxyethoxy)ethoxycarbonyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

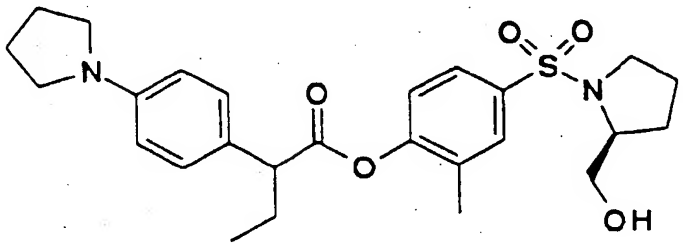


• HCl

NMR ($CDCl_3$): δ 7.69 (1H, s), 7.67 (2H, d, J=8.4Hz), 7.23 (2H, d, J=8.4Hz), 7.07 (1H, d, J=8.2Hz), 6.56 (2H, d, J=8.4Hz), 4.29 (3H, m), 3.75-3.58 (7H, m), 3.50 (1H, m), 3.29 (4H, m), 3.22 (1H, m), 2.16 (1H, m), 2.04 (3H, s), 2.01 (4H, m), 1.98-1.64 (5H, m), 0.99 (3H, t, J=7.2Hz);
TLC : Rf 0.62 (chloroform:methanol=9:1).

Example 2(10)

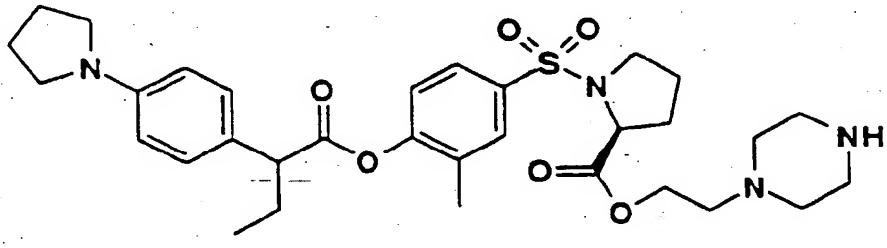
4-(2S-hydroxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70-7.58 (2H, m), 7.22 (2H, d, J=8.5Hz), 7.09 (1H, d, J=8.0Hz), 6.55 (2H, d, J=8.5Hz), 3.80-3.52 (3H, m), 3.62 (1H, t, J=7.5Hz), 3.52-3.35 (1H, m), 3.35-3.12 (5H, m), 2.90-2.55 (1H, brs), 2.35-1.70 (2H, m), 2.05 (3H, s), 2.05-1.95 (4H, m), 1.80-1.30 (4H, m), 0.99 (3H, t, J=7.5Hz);
TLC : Rf 0.36 (hexane:ethyl acetate=1:1).

Example 2(11)

4-(2S-(2-(piperazin-4-yl)ethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl) butanoic acid ester · 2hydrochloride



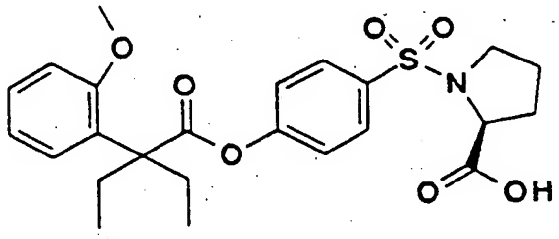
• 2HCl

NMR (CD_3OD): δ 7.82-7.63 (6H, m), 7.00 (1H, d, J=8.2Hz), 4.62 (2H, m), 4.41 (1H, m), 4.00 (1H, t, J=7.6Hz),

3.81-3.66 (8H, m), 3.57 (1H, m), 3.21 (1H, ml, 2.33 (7H, m), 2.07 (3H, s), 2.03-1.89 (5H, m), 1.69 (1H, m), 1.00(3H, t, J=7.4Hz);
TLC : Rf 0.48 (chloroform:methanol:water=40:10:1).

Example 2(12)

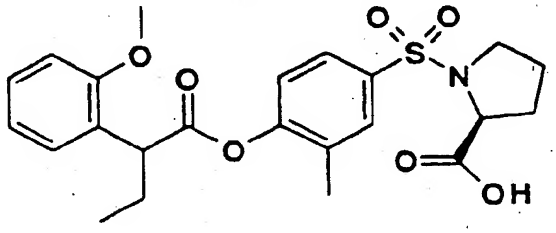
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2-(2-methoxyphenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 7.89 (2H, d, J=9Hz), 7.34-7.16 (4H, m), 7.06-6.95 (2H, m), 4.03 (1H, dd, J=2 and 8Hz), 3.82 (3H, s), 3.36-3.23 and 3.20-3.09 (each 1H, m), 2.23-1.91 (4H, m), 1.87-1.47 (4H, m), 0.72 (6H, t, J=7Hz);
TLC : Rf 0.19 (chloroform:methanol:water=9:1:0.1).

Example 2(13)

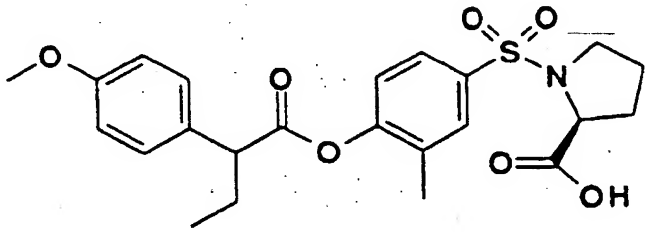
4-(2S-carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(2-methoxyphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.69 (1H, s), 7.68 (1H, d, J=9.0Hz), 7.35-7.22 (2H, m), 7.10 (1H, d, J=9.0Hz), 6.98 (1H, d, J=7.6Hz), 6.92 (1H, d, J=7.8Hz), 4.28-4.16 (1H, m), 4.15 (1H, t, J=7.6Hz), 3.85 (3H, s), 3.60-3.43 (1H, m), 3.26-3.07 (1H, m), 2.35-1.56 (4H, m), 2.04 (3H, s), 0.98 (3H, t, J=7.6Hz);
TLC : Rf 0.54 (chloroform:methanol:water=8:2:0.2).

Example 2(14)

4-(2S-carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester



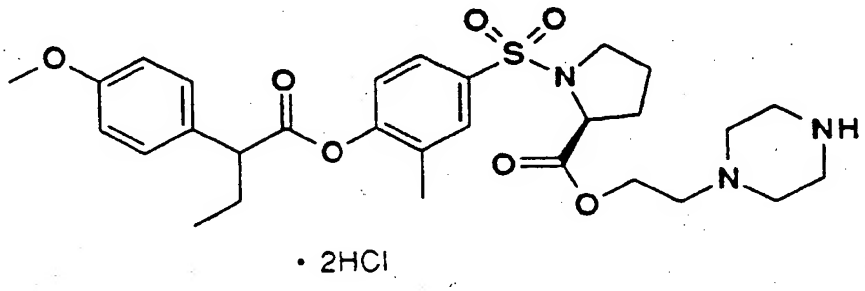
NMR (DMSO-d_6): δ 7.74 (1H, s), 7.69 (1H, d, J=8.2Hz), 7.33 (2H, d, J=8.8Hz), 7.17 (1H, d, J=8.2Hz), 6.95 (2H,

d, J=8.8Hz), 4.11 (1H, m), 4.14 (1H, m), 3.76 (3H, s), 3.30 (1H, m), 3.17 (1H, m), 2.10 (1H, m), 1.96 (3H, s), 1.82 (4H, m), 1.56 (1H, m), 0.91 (3H, t, J=7.2Hz);

TLC : Rf 0.58 (chloroform:methanol:acetic acid=12:1:1).

Example 2(15)

4-(2S-(2-(piperazin-1-yl)ethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester · 2hydrochloride



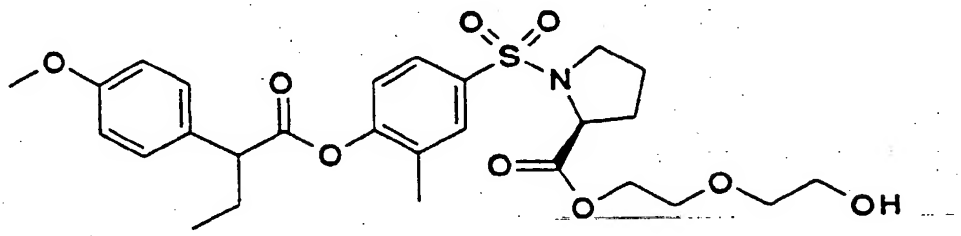
· 2HCl

NMR (CD_3OD): δ 7.77 (1H, s), 7.75 (1H, d, J=7.4Hz), 7.32 (2H, d, J=8.6Hz), 7.16 (1H, d, J=7.4Hz), 6.93 (2H, d, J=8.6Hz), 4.62 (2H, brs), 4.5-4.3 (1H, br), 3.8-3.4 (12H, br), 3.79 (3H, s), 3.3-3.1 (1H, br), 2.3-1.8 (6H, br), 2.00 (3H, s), 0.98 (3H, t, J=7.3Hz);

TLC : Rf 0.16 (chloroform:methanol:acetic acid=40:2:1).

Example 2(16)

4-(2S-(2-(2-hydroxyethoxy)ethoxycarbonyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester

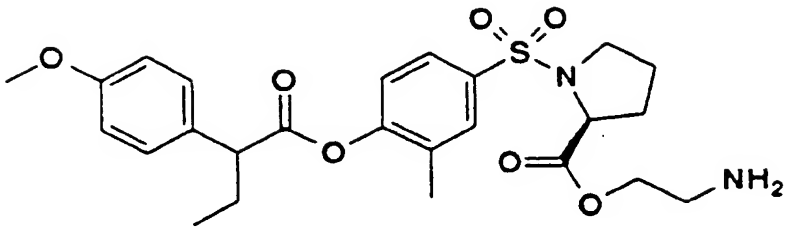


NMR ($CDCl_3$): δ 7.70 (1H, s), 7.68 (1H, d, J=8.8Hz), 7.31 (2H, d, J=8.4Hz), 7.01 (1H, d, J=8.8Hz), 6.90 (2H, d, J=8.4Hz), 4.3-4.2 (3H, m), 3.82 (3H, s), 3.8-3.7 (6H, m), 3.7-3.5 (2H, m), 3.3-3.2 (1H, m), 2.4-2.1 (2H, m), 2.00 (3H, s), 2.1-1.7 (4H, m), 0.99 (3H, t, J=7.3Hz);

TLC : Rf 0.24 (hexane:ethyl acetate=1:2).

Example 2(17)

4-(2S-(2-aminoethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester · hydrochloride

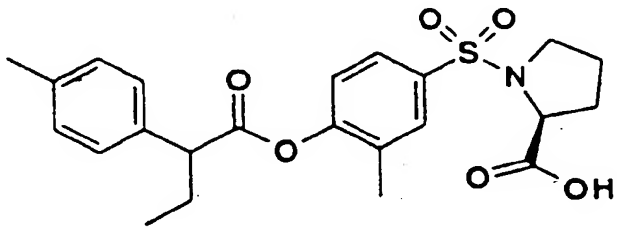


• HCl

NMR ($CDCl_3$): δ 8.40 (2H, brs), 7.73 (1H, s), 7.70 (1H, d, J=9.2Hz), 7.30 (2H, d, J=8.6Hz), 7.08 (1H, d, J=9.2Hz), 6.89 (2H, d, J=8.6Hz), 4.6-4.3 (3H, br), 3.80 (3H, s). 3.67 (1H, t, J=7.6Hz), 3.6-3.3 (3H, br), 3.2-3.1 (1H, br), 2.4-1.8 (6H, brj, 2.00 (3H, s), 0.98 (3H, t, J=7.3Hz);
TLC : Rf 0.23 (chloroform:methanol=9:1).

Example 2(18)

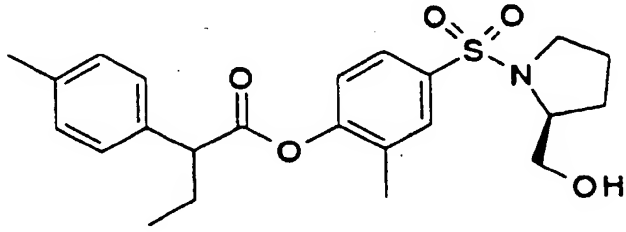
4-(2S-carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.69 (1H, s), 7.66 (1H, d, J=9.0Hz), 7.25 (2H, d, J=8.0Hz), 7.15 (2H, d, J=8.0Hz), 7.05 (1H, d, J=9.0Hz), 4.20 (1H, m), 3.67 (1H, t, J=8.0Hz), 3.60-3.40 (1H, m), 3.20-3.00 (1H, m), 2.34 (3H, s), 2.30-1.50 (6H, m), 1.96 (3H, s), 0.97 (3H, t, J=7.5Hz);
TLC : Rf 0.39 (acetic acid:methanol:chloroform=1:2:40).

Example 2(19)

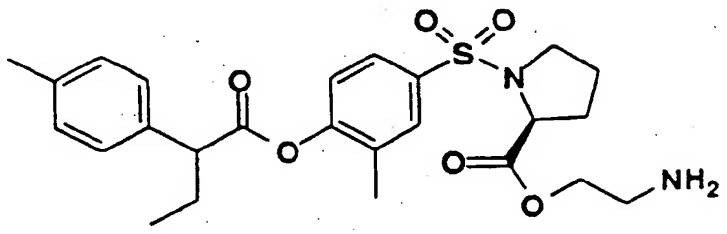
4-(2S-hydroxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.67 (1H, s), 7.65 (1H, d, J=8.0Hz), 7.28 (2H, d, J=8.0Hz), 7.18 (2H, d, J=8.0Hz), 7.09 (1H, d, J=8.0Hz), 3.70 (1H, t, J=7.5Hz), 3.74-3.54 (3H, m), 3.54-3.38 (1H, m), 3.30-3.14 (1H, m), 2.71 (1H, t-like), 2.36 (3H, s), 2.40-1.80 (2H, m), 2.02 (3H, s), 1.90-1.60 (3H, m), 1.60-1.40 (1H, m), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.23 (ethyl acetate:hexane=1:2).

Example 2(20)

4-(2S-(2-aminoethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester · hydrochloride

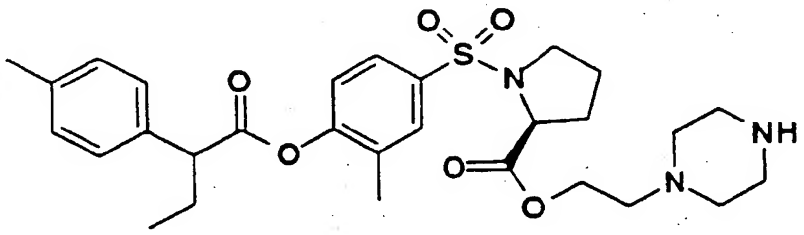


· HCl

NMR (DMSO-d_6): δ 8.22 (3H, brs), 7.75 (1H, d, J=1.8Hz), 7.70 (1H, dd, J=8.4 and 1.8Hz), 7.30 (2H, d, J=8.0Hz), 7.20 (3H, d, J=8.0Hz), 4.33-4.15 (1H, m), 4.26 (2H, t, J=5.0Hz), 3.85 (1H, t, J=7.6Hz), 3.49-3.01 (2H, m), 3.09 (2H, t, J=5.6Hz), 2.32 (3H, s), 2.25-1.50 (6H, m), 1.98 (3H, s), 0.92 (3H, t, J=7.2Hz);
TLC : Rf 0.56 (chloroform:methanol:acetic acid=15:2:1).

Example 2(21)

4-(2S-(2-(piperazin-4-yl)ethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester · 2hydrochloride

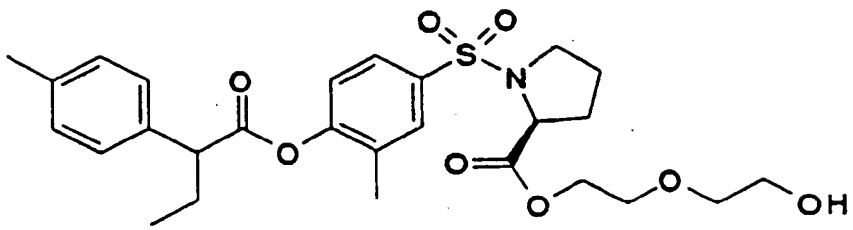


· 2HCl

NMR (CD_3OD): δ 7.78 (1H, s), 7.75 (1H, dd, J=8.6 and 1.2Hz), 7.29 (2H, d, J=8.0Hz), 7.24-7.12 (3H, m), 4.66-4.54 (2H, m), 4.45-4.32 (1H, m), 3.85-3.60 (11H, m), 3.60-3.38 (1H, m), 3.26-3.15 (1H, m), 2.34 (3H, s), 2.30-1.55 (6H, m), 1.99 (3H, s), 0.98 (3H, t, J=7.2Hz);
TLC : Rf 0.45 (chloroform:methanol:water=8:2:0.2).

Example 2(22)

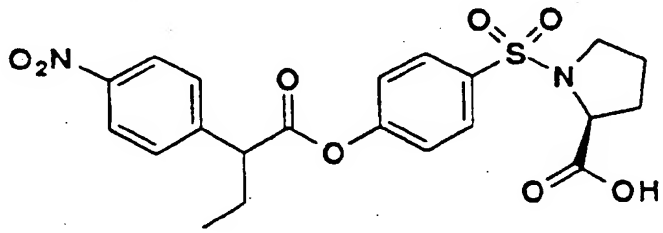
4-(2S-(2-(2-hydroxyethoxy)ethyl)oxycarbonyipyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70 (1H, s), 7.68 (1H, dd, J=7.4 and 2.4Hz), 7.28 (2H, d, J=8.2Hz), 7.18 (2H, d, J=8.2Hz), 7.07 (1H, d, J=8.8Hz), 4.40-4.20 (3H, m), 3.73-3.37 (8H, m), 3.37-3.16 (1H, m), 2.24-1.63 (6H, m), 2.36 (3H, s), 2.02 (3H, s, 1.70 (1H, s), 1.00 (3H, t, J=7.2Hz);
TLC : Rf 0.28 (ethyl acetate:hexane=2:1).

Example 2(23)

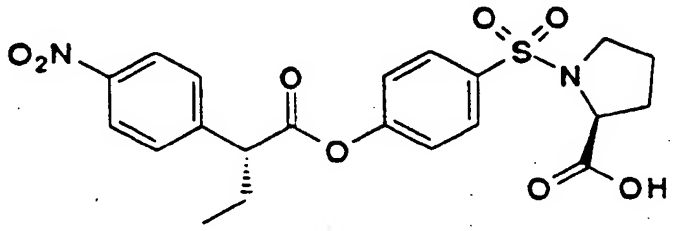
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR (DMSO-d_6): δ8.25 (2H, d, J=8Hz), 7.90 (2H, d, J=8Hz), 7.58 (2H, d, J=8Hz), 7.19 (2H, d, J=8Hz), 5.70-4.80 (1H, brs), 4.30 (1H, dd, J=7Hz, 4Hz), 3.85 (1H, t, J=7Hz), 3.60-3.39 (1H, m), 3.39-3.15 (1H, m), 2.45-1.65 (6H, m), 1.01 (3H, t, J=7Hz);
TLC : Rf 0.34 (acetic acid:methanol:chloroform=1:2:40).

Example 2(24)

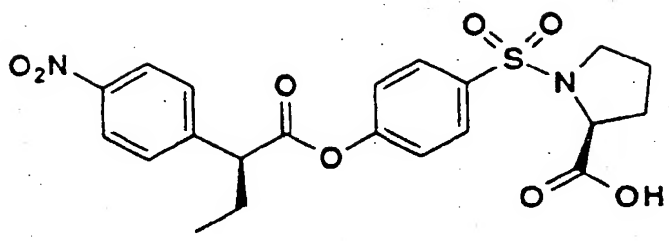
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2R-(4-nitrophenyl)butanoic acid ester



NMR ($CDCl_3$): δ 8.26 (d, J=8.8Hz, 2H), 7.90 (d, J=8.8Hz, 2H), 7.58 (d, J=8.8Hz, 2H), 7.20 (d, J=8.8Hz, 2H), 4.30 (dd, J=4.0, 7.8Hz, 1H), 3.86 (t, J=7.6Hz, 1H), 3.5-3.4 (m, 1H), 3.4-3.2 (m, 1H), 2.4-1.7 (m, 6H) 1.02 (t, J=7.3Hz, 3H);
TLC : Rf 0.63 (chloroform:methanol=6:1).

Example 2(25)

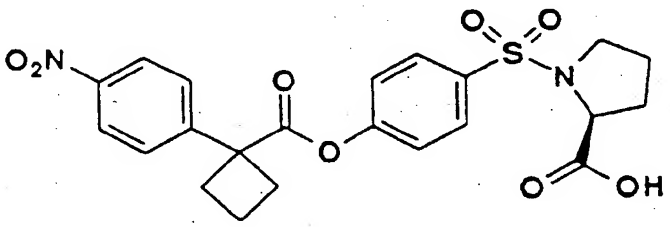
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2S-(4-nitrophenyl)butanoic acid ester



NMR ($CDCl_3$): δ8.26 (d, J=8.8Hz, 2H), 7.90 (d, J=8.8Hz, 2H), 7.58 (d, J=8.8Hz, 2H), 7.19 (d, J=8.8Hz, 2H), 4.31 (dd, J=4.0, 7.2Hz, 1H), 3.86 (t, J=7.7Hz, 1H), 3.6-3.4 (m, 1H), 3.4-3.2 (m, 1H), 2.4-1.7 (m, 6H), 1.03 (t, J=7.6Hz, 3H);
TLC : Rf 0.63 (chloroform:methanol=6:1).

Example 2(26)

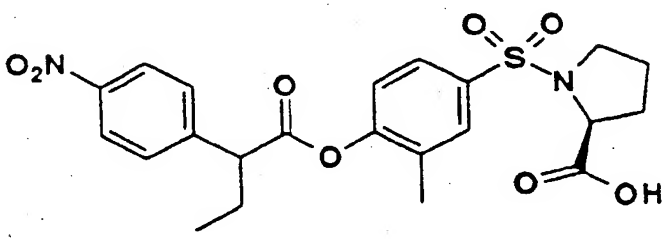
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 8.27 (2H, d, J=8Hz), 7.88 (2H, d, J=8Hz), 7.56 (2H, d, J=8Hz), 7.16 (2H, d, J=8Hz), 6.00-5.10 (1 H, brs), 4.29 (1 H, dd, J=7Hz, 4Hz), 3.55-3.40 (1H, m), 3.34-3.19 (1H, m), 3.15-2.98 (2H, m), 2.80-2.60 (2H, m), 2.38-1.66 (6H, m);
TLC : Rf 0.40 (acetic acid:methanol:chloroform=1:2:40).

Example 2(27)

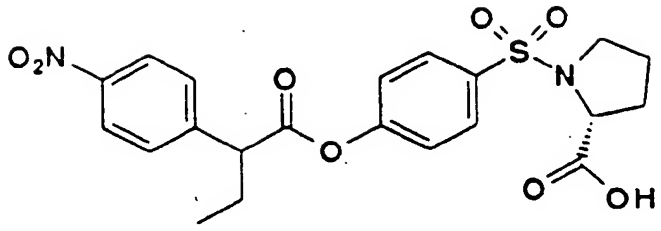
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 8.27 (2H, d, J=8.8Hz), 7.74 (2H, d, J=8.8Hz), 7.79-7.66 (2H, m), 7.23 (1H, d, J=8.4Hz), 4.20 (1H, t, J=7.6Hz), 4.12-4.06 (1H, m), 3.40-3.07 (2H, m), 2.35-1.40 (6H, m), 2.00 (3H, s), 0.92 (3H, t, J=7.2Hz);
TLC : Rf 0.19 (acetic acid:methanol:chloroform=1:2:40).

Example 2(28)

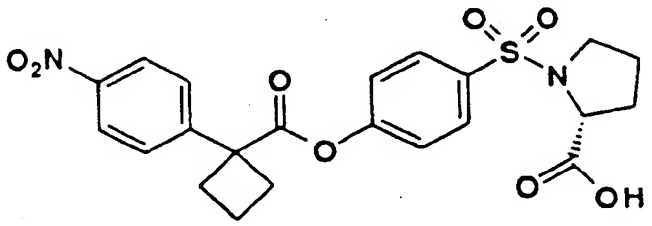
4-(2R-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 13.5-11.6 (1H, brs), 8.27 (2H, d, J=8.8Hz), 7.88 (2H, d, J=8.8Hz), 7.73 (2H, d, J=8.8Hz), 7.32 (2H, d, J=8.8Hz), 4,16 (1H, t, J=7.2Hz), 4.16-4.06 (1H, m), 3.5-3.0 (2H, m), 2.35-1.45 (6H, m), 0.92 (3H, t, J=7.2Hz);
TLC : Rf 0.43 (acetic acid:methanol:chloroform=1:2:40).

Example 2(29)

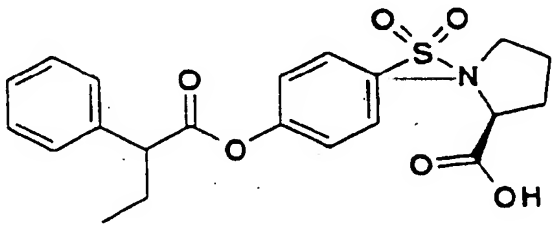
4-(2R-carboxypyrrolidin-1-ylsulfonyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 12.9-12.6 (1H, brs), 8.28 (2H, d, J=8.8Hz), 7.87 (2H, d, J=8.8Hz), 7.71 (2H, d, J=8.8Hz), 7.31 (2H, d, J=8.8Hz), 4.16-4.04 (1H, m), 3.43-3.10 (2H, m), 3.10-2.90 (2H, m), 2.75-2.55 (2H, q-like), 2.28-1.46 (6H, m);
TLC : Rf 0.46 (acetic acid:methanol:chloroform=1:2:40).

Example 2(30)

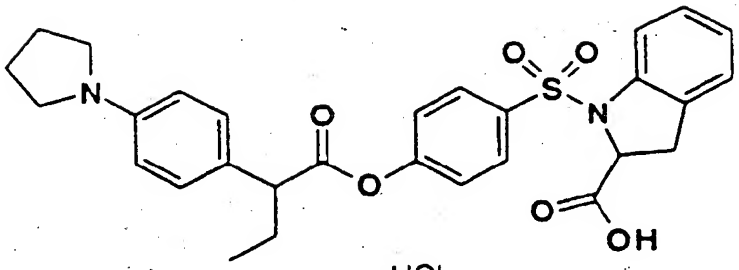
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.93-7.83 (2H, m), 7.50-7.14 (5H, m), 7.23-7.14 (2H, m), 7.14-6.70 (1H, brs), 4.26 (1H, dd, J=10Hz, 5Hz), 3.71 (1H, t, J=7Hz), 3.56-3.43 (1H, m), 3.33-3.17 (1H, m), 2.35-1.65 (6H, m), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.67 (acetic acid-methanol:chloroform=1:3:30).

Example 2(31)

4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

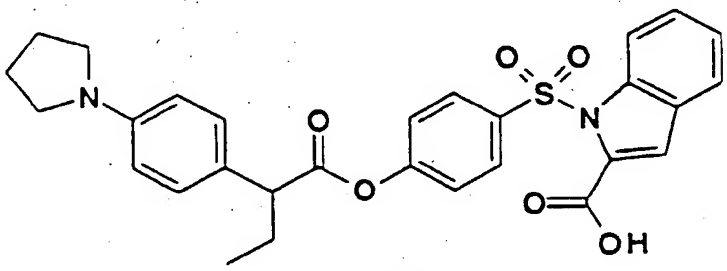


• HCl

NMR ($CDCl_3$): δ 7.73 (2H, d, J=8.6Hz), 7.58 (1H, d, J=8.2Hz), 7.17 (2H, d, J=8.6Hz), 7.12-6.94 (5H, m), 6.53 (2H, d, J=8.8Hz), 4.73 (1H, dd, J=8.9Hz and 6.8Hz), 3.54 (1H, t, J=7.8Hz), 3.35-3.21 (4H, m), 3.17 (2H, d, J=6.8Hz), 2.25-1.70 (2H, m), 2.05-1.94 (4H, m), 0.95 (3H, t, J=7.2Hz);
TLC : Rf 0.46 (acetic acid:methanol:chloroform=1:2:40).

Example 2(32)

4-(2-carboxyindol-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

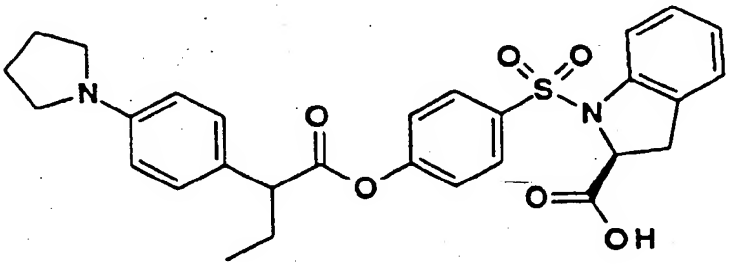


• HCl

NMR ($DMSO-d_6$): δ 8.08 (2H, d, J=8.8Hz), 8.01 (1H, d, J=8.4Hz), 7.68 (1H, d, J=8.0Hz), 7.46 (1H, m), 7.40-7.16 (2H, m), 7.24 (2H, d, J=8.8Hz), 7.20 (2H, d, J=8.6Hz), 6.85-6.60 (2H, m), 3.69 (1H, t, J=7.4Hz), 3.40-3.15 (4H, m), 2.20-1.84 (5H, m), 1.84-1.60 (1H, m), 0.86 (3H, t, J=7.4Hz);
TLC : Rf 0.20 (chloroform:methanol:water=9:1:0.1).

Example 2(33)

4-(2S-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

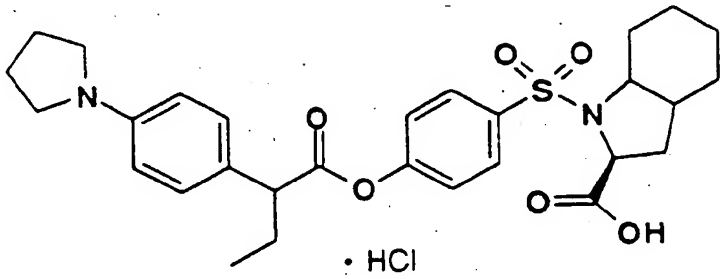


NMR ($CDCl_3$): δ 7.72 (2H, d, J=8.6Hz), 7.57 (1H, d, J=7.8Hz), 7.17 (2H, d, J=8.6Hz), 7.28-6.88 (5H, m), 6.53 (2H, d, J=8.6Hz), 4.72 (1H, dd, J=5.8Hz and 9.1Hz), 3.54 (1H, t, J=7.8Hz), 3.35-3.22 (4H, m), 3.22-3.08 (2H, m),

2.25-1.70 (2H. m), 2.05-1.95 (4H, m), 0.95 (3H, t, J=7.2Hz);
TLC : Rf 0.46 (acetic acid:methanol:chloroform=1:2:40).

Example 2(34)

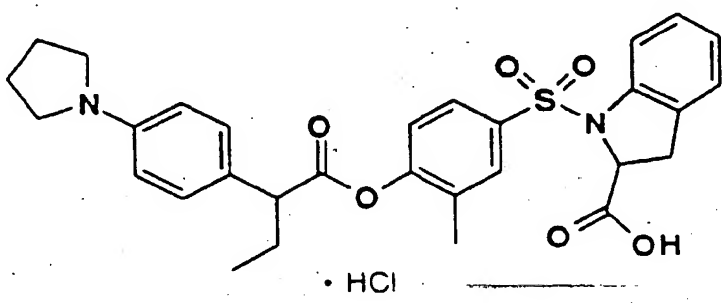
4-(2S-carboxyperhydroindol-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ 7.89 (2H, d, J=8.8Hz), 7.71 (2H, d, J=8.6Hz), 7.51 (2H, d, J=8.6Hz), 7.17 (2H, d, J=8.8Hz), 4.20 (1H, t, J=8.6Hz), 4.0-3.5 (6H, m), 2.5-2.2 (4H, m), 2.4-1.0 (13H, m), 0.99 (3H, t, J=7.4Hz);
TLC : Rf 0.60 (chloroform:methanol:acetic acid=40:2:1).

Example 2(35)

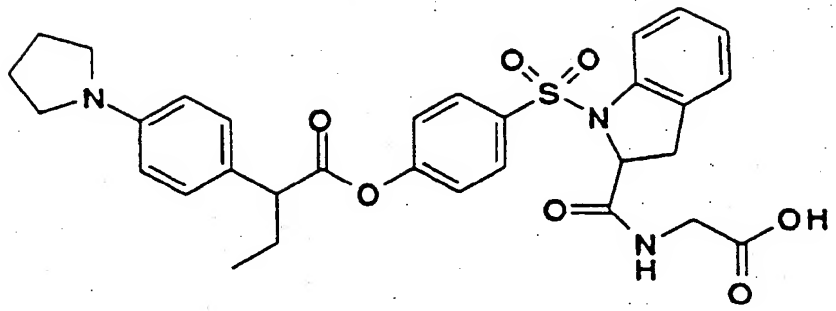
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($DMSO-d_6$): δ 7.79 (1H, d-like), 7.67 (1H, dd, J=2.2 and 8.4Hz), 7.35-6.95 (7H, m), 6.71-6.67 (2H, m), 4.97 (1H, dd, J=4.4 and 10.7Hz), 3.71 (1H.t, J=7.6Hz), 3.35-2.96 (6H, m), 2.14-1.68 (2H, m), 2.00-1.94 (4H, m), 1.91 (3H, s), 0.87 (3H, t, J=7.2Hz);
TLC : Rf 0.45 (chloroform:methanol:water=8:2:0.2).

Example 2(36)

4-(2RS-(N-carboxymethylcarbamoyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

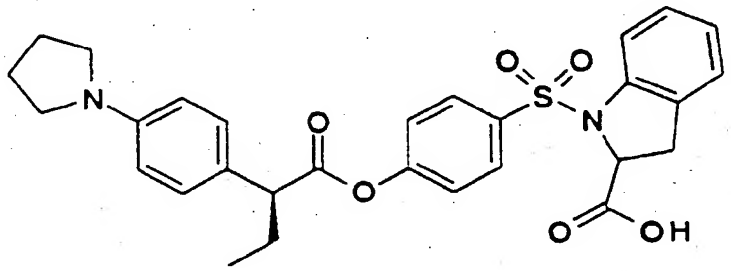


NMR ($CDCl_3$) : δ 7.70 (1H, d, J=7.8Hz), 7.58 (2H, d, J=8.8Hz), 7.28-7.02 (8H, m), 6.66 (2H, d, J=8.8Hz), 4.64 (1H, dd, J=10.4, 2.8Hz), 4.02 (2H, d, J=3.0Hz), 3.56 (1H, t, J=7.6Hz), 3.37-3.05 (5H, m), 2.81 (1H, dd, J=16.0, 10.4Hz), 2.35-1.74 (6H, m), 0.95 (3H, t, J=7.6Hz);

TLC : Rf 0.33 (chloroform:methanol:acetic acid=40:2:1).

Example 2(37)

4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

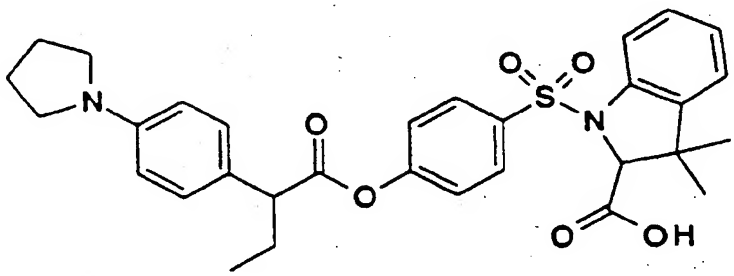


NMR ($CDCl_3$): δ 7.72 (2H, d, J=8Hz), 7.59 (1H, d, J=8Hz), 7.27-7.03 (7H, m), 6.54 (2H, d, J=8Hz), 6.08 (1H, br), 4.77-4.69 (1H, m), 3.55 (1H, t, J=8Hz), 3.31-3.24 (4H, m), 3.19-3.15 (2H, m), 2.20-1.76 (2H, m), 2.03-1.96 (4H, m), 0.95 (3H, t, J=8Hz);

TLC : Rf 0.45 (chloroform:methanol:water=8:2:0.2).

Example 2(38)

4-(2RS-carboxy-3,3-dimethylindolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

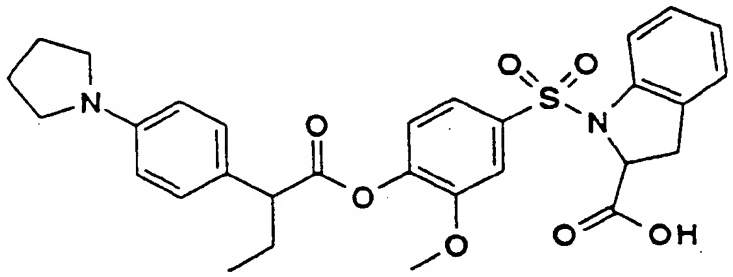


NMR ($CDCl_3$): δ 7.83 (2H, d, J=8.5Hz), 7.55 (1H, d, J=8.0Hz), 7.25-6.93 (3H, m), 7.17 (2H, d, J=8.5Hz), 7.09 (2H, d, J=8.5Hz), 6.53 (2H, d, J=8.5Hz), 4.36 (1H, s), 3.54 (1H, t, J=8.0Hz), 3.35-3.10 (4H, m), 2.05-1.90 (4H, m), 2.25-1.70 (2H, m), 1.31 (3H, s), 1.04 (3H, s), 0.94 (3H, t, J=7.5Hz);

TLC : Rf 0.48 (chloroform:methanol:acetic acid=40:2:1).

Example 2(39)

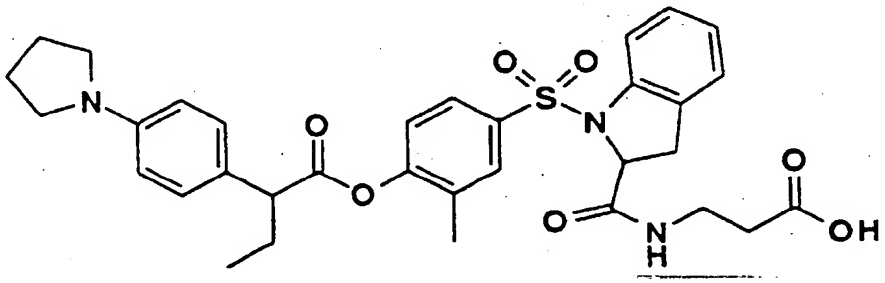
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methoxyphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.7-7.6 (m, 1H), 7.5-6.9 (m, 8H), 6.5-6.4 (m, 2H), 4.8-4.6 (m, 1H), 3.8-3.5 (m, 4H), 3.4-3.0 (m, 6H), 2.2-1.7 (m, 6H), 1.1-0.9 (m, 3H);
TLC : Rf 0.65 (chloroform:methanol=3:1).

Example 2(40)

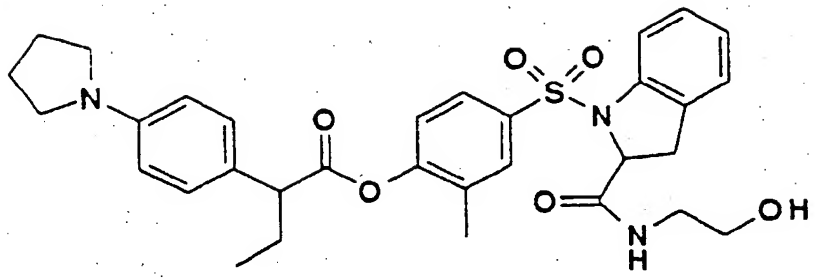
4-(2RS-(N-2-carboxyethylcarbamoyl)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.8-6.8 (m, 11H), 4.7-4.5 (m, 1H), 3.8-3.5 (m, 7H), 3.3-3.1 (m, 1H), 3.0-2.8 (m, 1H), 2.7-2.5 (m, 2H), 2.3-2.1 (m, 4H), 2.1-1.8 (m, 5H), 0.97 (t, J=7.2Hz, 3H);
TLC : Rf 0.76 (methanol:chloroform=1:3).

Example 2(41)

4-(2RS-(N-2-hydroxyethylcarbamoyl)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

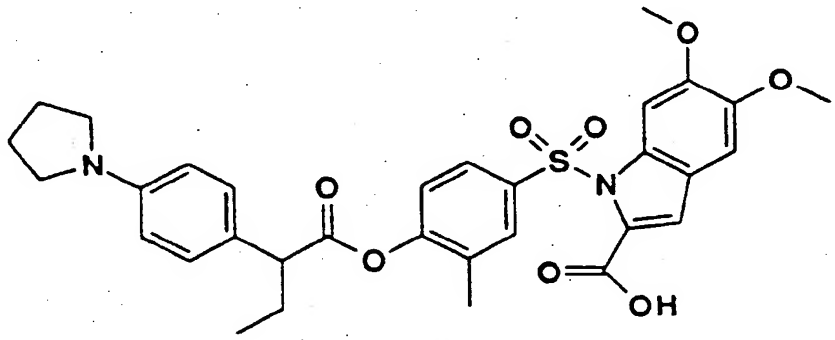


NMR ($CDCl_3$): δ 7.72 (1H, d, J=8.0Hz), 7.45-6.92 (9H, m), 6.51 (2H, d, J=8.6Hz), 4.57 (1H, dd, J=2.8, 10.6Hz), 3.77-3.52 (5H, m), 3.39-3.17 (5H, m), 2.88 (1H, dd, J=10.6, 16.8Hz), 2.23-1.78 (6H, m), 1.92 (3H, s), 0.96 (3H, t, J=7.4Hz);

TLC : Rf 0.43 (chloroform:methanol:acetic acid=25:5:1).

Example 2(42)

4-(2-carboxy-5,6-dimethoxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

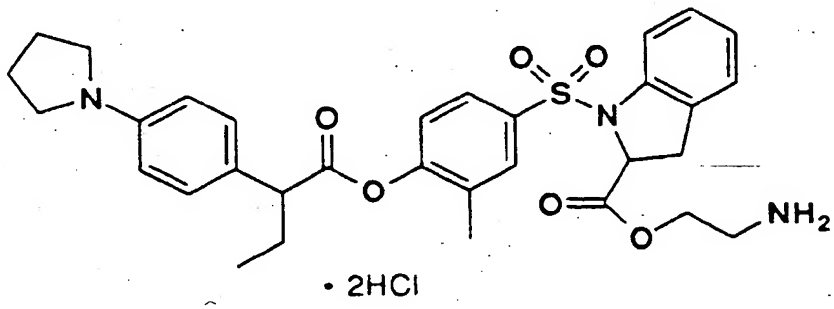


NMR ($CDCl_3$): δ 7.78-7.62 (3H, m), 7.35 (1H, s), 7.18 (2H, d, J=9Hz), 7.00 (1H, d, J=8Hz), 6.95 (1H, s), 6.52 (2H, d, J=9Hz), 4.00 (3H, s), 3.91 (3H, s), 3.70-3.10 (1H, brs), 3.57 (1H, t, J=7Hz), 3.35-3.18 (4H, m), 2.25-1.75 (9H, m), 0.96 (3H, t, J=7Hz).

TLC : Rf 0.19 (ethyl acetate:hexane:acetic acid=5:10:0.5).

Example 2(43)

4-(2RS-(2-aminoethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

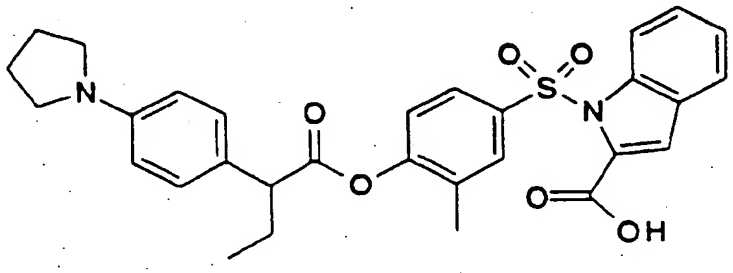


NMR (DMSO-d_6): δ 8.30 (2H, brs), 7.76 (1H, s), 7.66 (1H, d, J=8.0Hz), 7.37 (1H, d, J=8.0Hz), 7.23-7.00 (6H, m), 6.70 (2H, d, J=8.0Hz), 5.08 (1H, dd, J=6.2, 9.4Hz), 4.37-4.32 (2H, m), 3.69 (1H, t, J=7.2Hz), 3.35-3.07 (8H, m), 2.14-1.69 (9H, m), 0.89 (3H, t,J=7.2Hz);

TLC : Rf 0.46 (chloroform:methanol:acetic acid=25:5:1).

Example 2(44)

4-(2-carboxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

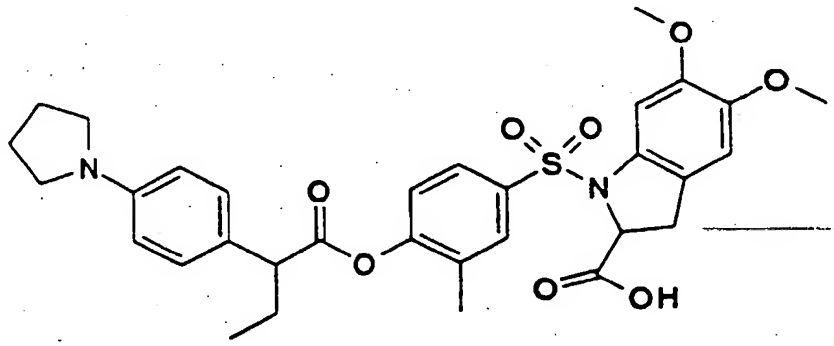


NMR ($CDCl_3$): δ 8.13 (1H, d, J=9Hz), 7.90-7.78 (2H, m), 7.60 (1H, d, J=9Hz), 7.46 (1H, td, J=8.1Hz), 7.39 (1H, s), 7.35-7.25 (1H, m), 7.21 (2H, d, J=9Hz), 6.75-6.50 (2H, m), 3.59 (1H, t, J=7Hz), 3.38-3.23 (4H, m), 3.23-2.90 (1H, brs), 2.25-1.75 (6H, m), 0.96 (3H, t, J=7Hz);

TLC : Rf 0.20 (ethyl acetate:hexane:acetic acid=5:10:0.5).

Example 2(45)

4-(2RS-carboxy-5,6-dimethoxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

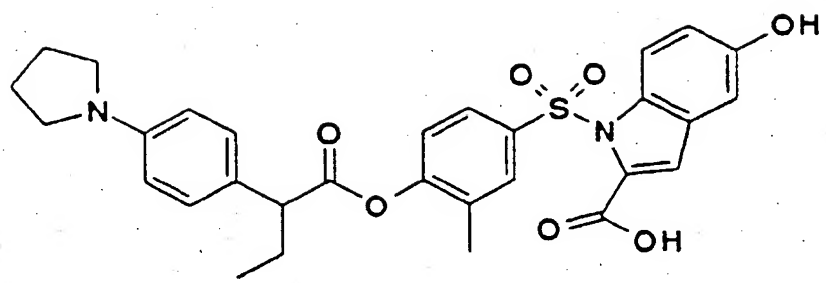


NMR ($CDCl_3$+CD_3OD): δ 7.6-7.4 (m, 2H), 7.26 (s, 1H), 7.19 (d, J=8.7Hz, 2H), 6.96 (dd, J=1.2, 8.4Hz, 1H), 6.58 (s, 1H), 6.54 (d, J=8.7Hz, 2H), 4.7-4.6 (m, 1H), 3.91 (s, 3H), 3.79 (s, 3H), 3.58 (t, J=7.7Hz, 1H), 3.4-3.2 (m, 4H), 3.1-2.9 (m 2H), 2.3-1.8 (m, 6H), 1.94 (s, 3H), 0.96 (t, J=7.4Hz, 3H);

TLC : Rf 0.45 (chloroform:methanol=4:1).

Example 2(46)

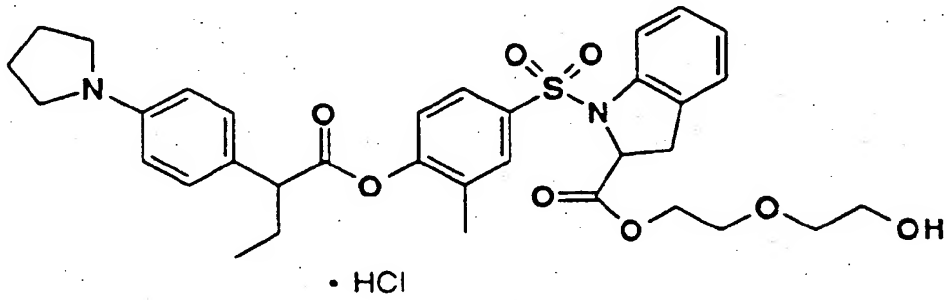
4-(2-carboxy-5-hydroxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (CD_3OD): δ 7.85-7.63 (3H, m), 7.03 (2H, d, J=8Hz), 6.93 (1H, d, J=8Hz), 6.87-6.70 (3H, m), 6.53 (2H, d, J=8Hz), 3.56 (1H, t, J=7Hz), 3.30-3.10 (4H, m), 2.20-1.90 (5H, m), 1.90-1.65 (1H, m), 1.84 (3H, s), 0.91 (3H, t, J=7Hz);
TLC : Rf 0.23 (ethyl acetate:hexane:acetic acid=10:10:0.5).

Example 2(47)

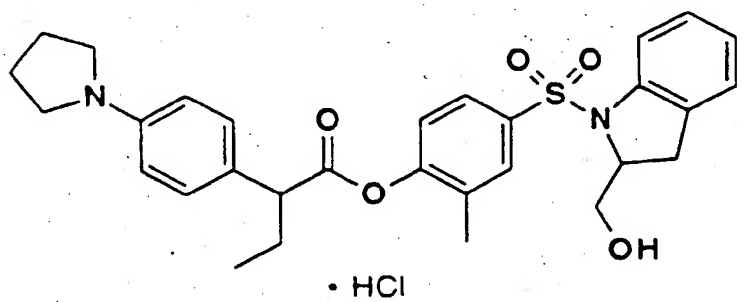
4-(2RS-(2-(2-hydroxyethoxy)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ 7.61-7.51 (3H, m), 7.23-7.10 (3H, m), 7.10-6.95 (3H, m), 6.51 (2H, d, J=8.0Hz), 4.75 (1H, dd, J=5.6, 10.2Hz), 4.38-4.33 (2H, m), 3.75-3.51 (7H, m), 3.30-3.22 (5H, m), 3.09 (1H, dd, J=5.6, 16.6Hz), 2.23-1.78 (6H, m), 1.96 (3H, s). 0.96 (3H, t, J=7.4Hz);
TLC : Rf 0.65 (chloroform:methanol=15:1).

Example 2(48)

4-(2RS-hydroxymethylindolin-1-ylsulfonyl)-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

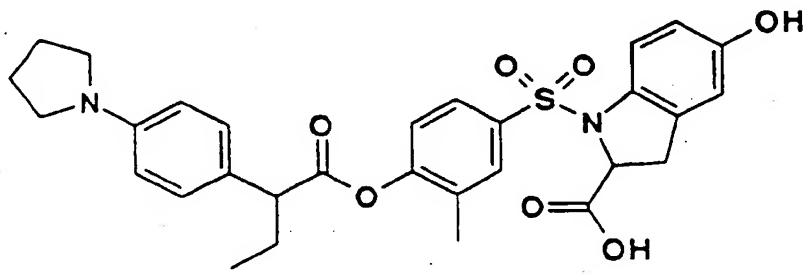


NMR (DMSO-d_6): δ 7.60 (1H, s-like), 7.51.7.40 (2H, m), 7.22-6.97 (6H, m), 6.51 (2H, d, J=8Hz), 4.40-4.24 (1H,

m), 3.68-3.37 (3H, m), 3.65 (1H, t, J=7Hz), 3.23-3.17 (4H, m), 2.87-2.69 (2H, m), 2.19-1.62 (each 1H, m), 1.99-1.93 (4H, m), 1.86 (3H, s), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.29 (hexane:ethyl acetate=2:1).

Example 2(49)

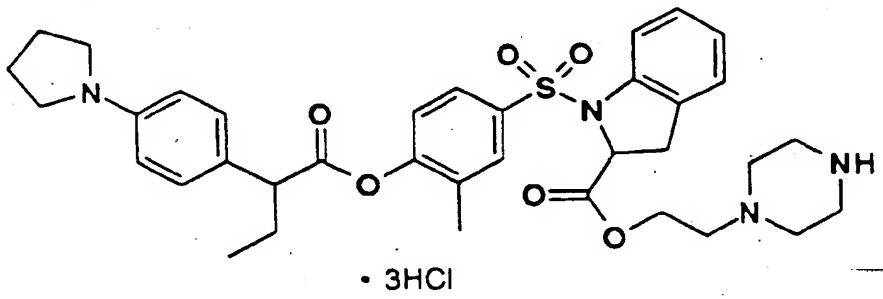
4-(2RS-carboxy-5-hydroxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$+3 drops of CD_3OD): δ 7.5-7.4 (m, 3H), 7.2-7.1 (m, 3H), 7.0-6.9 (m, 1H), 6.5-6.4 (m, 3H), 4.7-4.6 (m, 1H), 3.58 (t, J=7.8Hz, 1H), 3.4-3.2 (m, 4H), 3.1-2.9 (m, 2H), 2.2-1.8 (m, 6H), 1.94 (s, 3H), 0.97 (t, J=7.2Hz, 3H);
TLC : Rf 0.2 (chloroform:methanol=6:1).

Example 2(50)

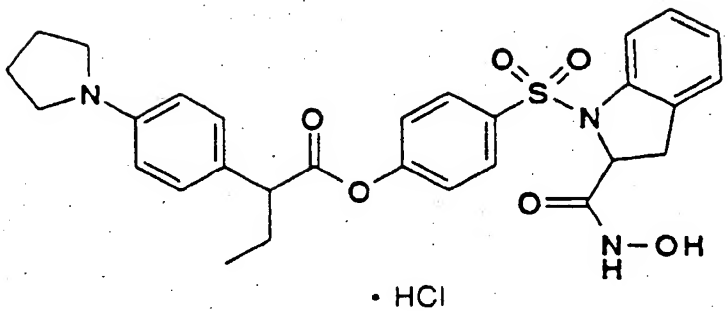
4-(2RS-(2-(piperazin-1-yl)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl) butanoic acid ester · 3hydrochloride



NMR (CD_3OD): δ 7.72-7.64 (3H, m), 7.57-7.49 (4H, m), 7.26-7.00 (4H, m), 5.12 (1H, dd, J=6.0, 8.8Hz), 4.63-4.59 (2H, m), 3.90 (1H, t, J=8.0Hz), 3.77-3.59 (14H, m), 3.23-3.20 (2H, m), 2.32-1.83 (6H, m), 1.96 (3H, s), 0.97 (3H, t, J=7.4Hz);
TLC : Rf 0.41 (chloroform:methanol:acetic acid=25:5:1).

Example 2(51)

4-(2RS-(N-hydroxycarbamoyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

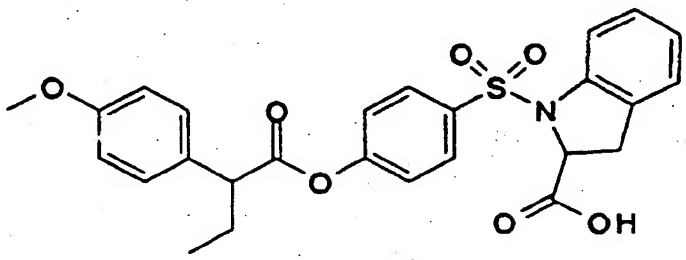


• HCl

NMR (CD_3OD): δ 7.75 (2H, d, J=8.6Hz), 7.60 (1H, d, J=8.0Hz), 7.58-7.48 (4H, m), 7.21 (1H, dd, J=6.5Hz, 1.5Hz), 7.12 (2H, d, J=8.6Hz), 7.09-7.01 (2H, m), 4.68 (1H, dd, J=9.0Hz, 5.0Hz), 3.87 (1H, t, J=7.0Hz), 3.77-3.70 (4H, m), 3.03-2.98 (2H, m), 2.28-2.23 (4H, m), 2.20-2.13 (0.5H, m), 1.97-1.81 (1.5H, m), 0.90 (3H, t, J=7.0Hz);
TLC : Rf 0.49 (hexane:ethyl acetate:acetic acid=8:8:1).

Example 2(52)

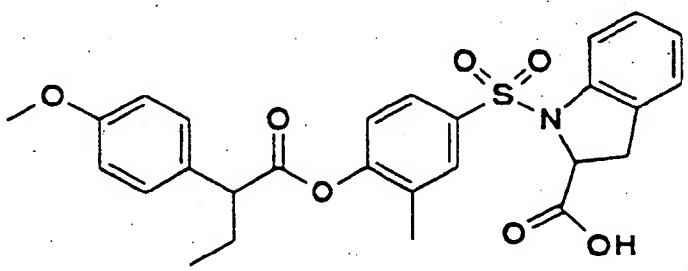
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-methoxyphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.74 (2H, d, J=8.8Hz), 7.58 (1H, d, J=8.0Hz), 7.29-7.02 (7H, m), 6.87 (2H, d, J=8.8Hz), 4.90 (1H, brs), 4.73 (1H, dd, J=9.2, 5.8Hz), 3.80 (3H, s), 3.60 (1H, t, J=7.8Hz), 3.20-3.15 (2H, m), 2.23-2.05 (1H, m), 1.94-1.76 (1H, m), 0.951 (3H, t, J=7.6Hz);
TLC : Rf 0.36 (chloroform:methanol:acetic acid=40:2:1).

Example 2(53)

4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester

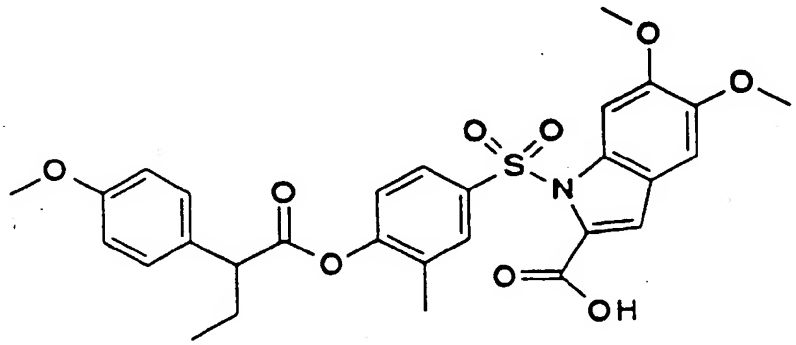


NMR (DMSO-d_6): δ 7.82 (1H, d-like), 7.72 (1H, d-like), 7.38 (2H, d, J=8.6Hz), 7.32 (1H, d, J=7.8Hz), 7.23-7.10 (3H, m), 7.03-6.96 (3H, m), 4.73 (1H, dd, J=5.2 and 9.3Hz), 3.88 (1H, t, J=7.6Hz), 3.82 (3H, s), 3.14-3.05 (2H, m), 2.25-2.10 and 1.96-1.79(each 1H, m), 0.96 (3H, t, J=7.2Hz);

TLC : Rf 0.41 (chloroform:methanol:water=8:2:0.2).

Example 2(54)

4-(2-carboxy-5,6-dimethoxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester

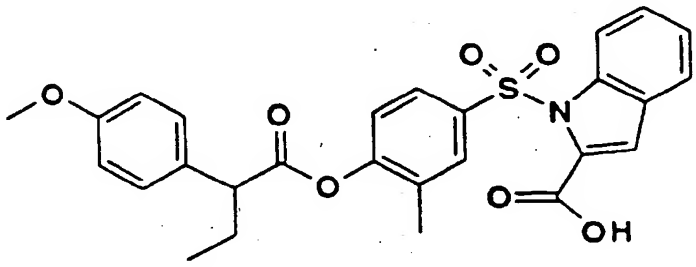


NMR ($CDCl_3$): δ 7.79-7.64 (3H, m), 7.36 (1H, s), 7.23 (2H, d, J=9Hz), 7.01 (1H, d, J=9Hz), 6.96 (1H, s), 6.88 (2H, d, J=9Hz), 4.00 (3H, s), 3.91 (3H, s), 3.80 (3H, s), 3.64 (1H, t, J=7Hz), 2.27-2.03 (1H, m), 2.00-1.80 (1H, m), 1.96 (3H, s). 0.96 (3H, t, J=7Hz);

TLC : Rf 0.10 (ethyl acetate:hexane:acetic acid=5:10:0.5).

Example 2(55)

4-(2-carboxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester

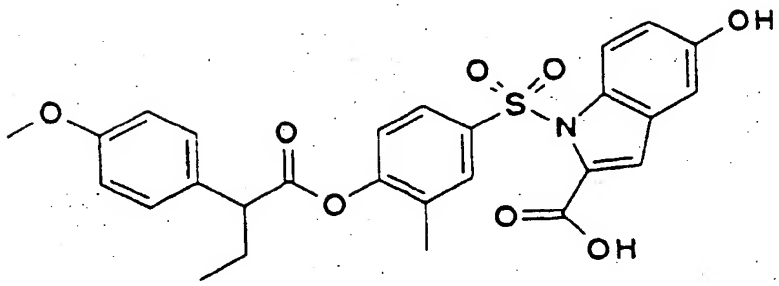


NMR ($CDCl_3$): δ 8.14 (1H, d, J=9Hz), 7.90-7.78 (2H, m), 7.60 (1H, d, J=9Hz), 7.52-7.40 (1H, m), 7.38 (1H, s), 7.35-7.20 (3H, m), 7.03 (1H, d, J=9Hz), 6.87 (2H, d, J=9Hz), 3.79 (3H, s), 3.64 (1H, t, J=7Hz), 2.28-2.05 (1H, m), 2.00-1.79 (1H, m), 1.96 (3H, s), 0.96 (3H, t, J=7Hz);

TLC : Rf 0.26 (ethyl acetate:hexane:acetic acid=5:10:0.5).

Example 2(56)

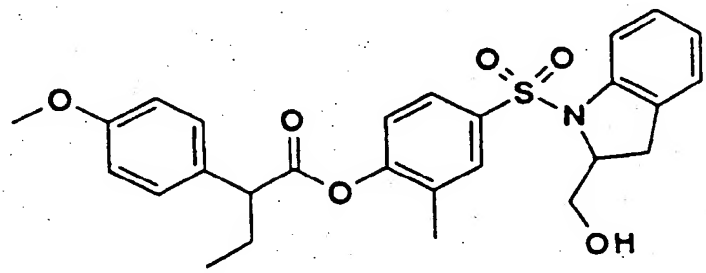
4-(2-carboxy-5-hydroxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.94 (1H, d, J=9Hz), 7.80-7.69 (2H, m), 7.26 (2H, d, J=9Hz), 7.17 (1H, s), 6.99 (1H, d, J=9Hz), 6.96 (1H, dd, J=9,2Hz), 6.87 (2H, d, J=9Hz), 6.87 (1H, d, J=2Hz), 3.80-3.40 (1H, brs), 3.79 (3H, s), 3.64 (1H, t, J=7Hz), 2.26-2.05 (1H, m), 2.00-1.75 (1H, m), 1.93 (3H, s), 0.95 (3H, t, J=7Hz);
TLC : Rf 0.16 (ethyl acetate:hexane:acetic acid=10:10:0.5).

Example 2(57)

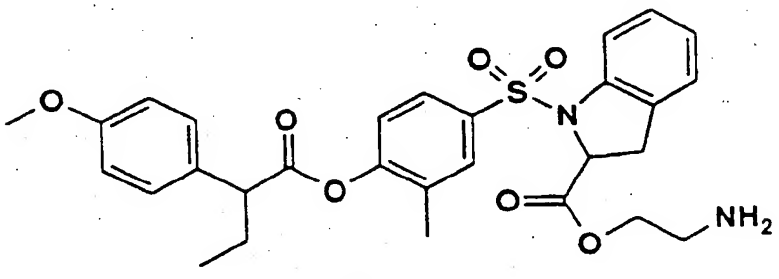
4-(2RS-hydroxymethylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester



NMR ($DMSO-d_6$): δ 7.61 (1H, s-like), 7.50-7.40 (2H, m), 7.28 (2H, d, J=8Hz), 7.21-6.96 (4H, m), 6.92 (2H, d, J=8Hz), 5.02 (1H, t-like), 4.32 (1H, m) 3.78 (1H, t, J=7Hz), 3.74 (3H, s), 3.67-3.57 and 3.47-3.37 (each 1H, m), 2.83-2.70 (2H, m), 2.10-1.95 and 1.86-1.65 (each 1H, m), 1.85 (3H, s), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.21 (hexane:ethyl acetate=2:1).

Example 2(58)

4-(2RS-(2-aminoethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester · hydrochloride



· HCl

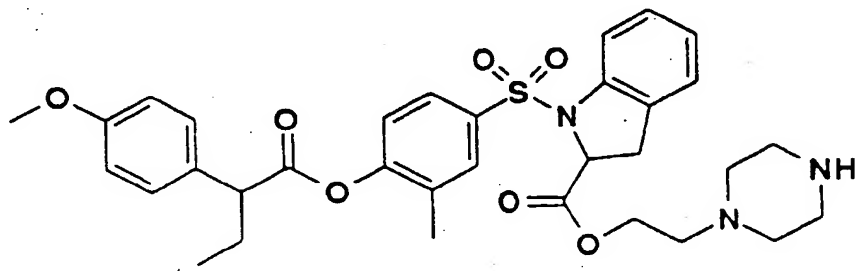
NMR ($DMSO-d_6$): δ 8.25 (3H, brs), 7.78-7.65 (2H, m), 7.39-7.00 (5H, m), 7.28 (2H, d, J=8.8Hz), 6.91 (2H, d,

J=8.8Hz), 5.08 (1H, dd, J=5.8, 10.0Hz), 4.34 (2H, t, J=5.2Hz), 3.83-3.74 (1H, m), 3.74 (3H, s), 3.30-3.09 (4H, m), 2.17-1.75 (2H, m), 1.90 (3H, s), 0.89 (3H, t, J=7.2Hz);

TLC : Rf 0.53 (chloroform:methanol:acetic acid=25:5:1).

Example 2(59)

4-(2RS-(2-(piperazin-4-yl)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester · 2hydrochloride



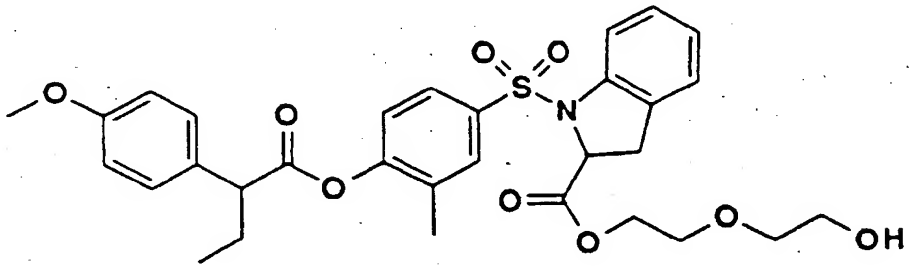
· 2HCl

NMR (CD_3OD) : δ 7.68-7.63 (2H, m), 7.51 (1H, d, J=7.8Hz), 7.27 (2H, d, J=8.4Hz), 7.22-7.02 (4H, m), 6.90 (2H, d, J=8.4Hz), 5.10 (1H, t, J=7.2Hz), 4.60 (2H, brs), 3.78 (3H, s), 3.75-3.19 (13H, m), 2.23-1.78 (2H, m), 1.89 (3H, s), 0.95 (3H, t, J=7.4Hz);

TLC : Rf 0.16 (chloroform:methanol=10:1).

Example 2(60)

4-(2RS-(2-(2-hydroxyethoxy)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester

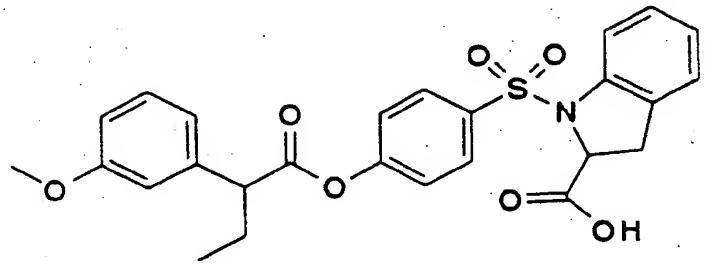


NMR ($CDCl_3$): δ 7.62-7.51 (3H, m), 7.26 (2H, d, J=8.4Hz), 7.28-6.96 (4H, m), 6.87 (2H, d, J=8.4Hz), 4.76 (1H, dd, J=5.4, 10.6Hz), 4.38-4.34 (2H, m), 3.80 (3H, s), 3.75-3.55 (7H, m), 3.31-3.04 (2H, m), 2.26-1.80 (2H, m), 1.93 (3H, s), 0.97 (3H, t, J=7.4Hz);

TLC : Rf 0.11(hexane:ethyl acetate=1:1).

Example 2(61)

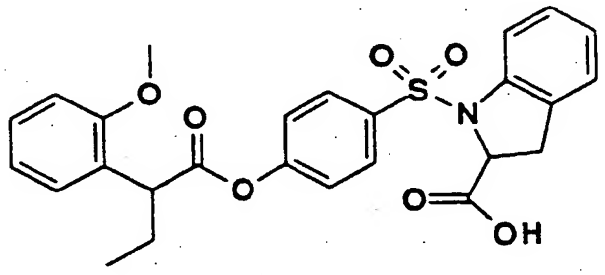
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(3-methoxyphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.75 (2H, d, J=8.8Hz), 7.57 (1H, d, J=7.8Hz), 7.30-6.79 (9H, m), 4.73 (1H, t, J=8.0Hz), 3.80 (3H, s), 3.62 (1H, t, J=7.8Hz), 3.20-3.17 (2H, m), 2.28-2.05 (1H, m), 1.99-1.77 (1H, m), 0.96 (3H, t, J=7.4Hz);
TLC : Rf 0.66 (chloroform:methanol:acetic acid=40:2:1).

Example 2(62)

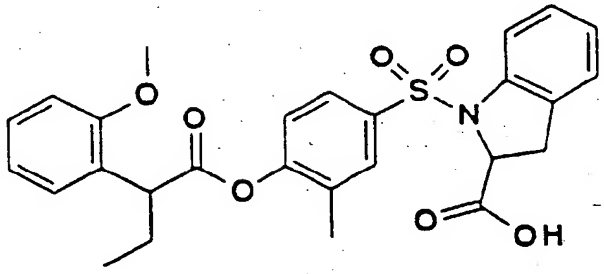
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(2-methoxyphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.75 (2H, d, J=8.8Hz), 7.58 (1H, d, J=8.0Hz), 7.25 (2H, d, J=8.8Hz), 7.31-6.87 (7H, m), 4.74 (1H, t, J=8.0Hz), 4.04 (1H, t, J=7.2Hz), 3.84 (3H, s), 3.18 (2H, brd, J=7.2Hz), 2.22-2.05 (1H, m), 1.96-1.74 (1H, m), 0.95 (3H, t, J=7.6Hz);
TLC : Rf 0.48 (chloroform:methanol:acetic acid=40:2:1).

Example 2(63)

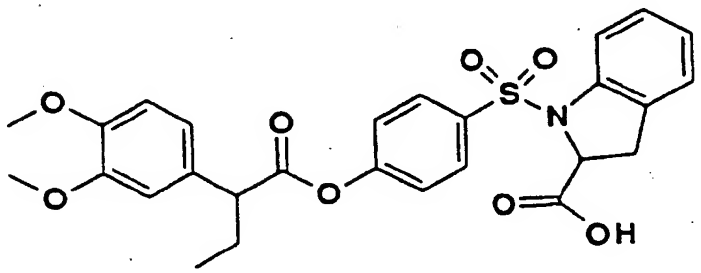
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(2-methoxyphenyl)butanoic acid ester



NMR ($DMSO-d_6$): δ 13.19 (1H, br), 7.79 (1H, d, J=2.0Hz), 7.68 (1H, dd, J=2.0 and 8.5Hz), 7.36-6.92 (9H, m), 4.96 (1H, dd, J=4.2 and 10.9Hz), 4.08 (1H, t, J=7.6Hz), 3.80 (3H, s), 3.39-2.96 (2H, m), 2.19-1.69 (2H, m), 1.95 (3H, s), 0.87 (3H, t, J=7.2Hz);
TLC : Rf 0.39 (chloroform:methanol:water=8:2:0.2).

Example 2(64)

4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(3,4-dimethoxyphenyl)butanoic acid ester

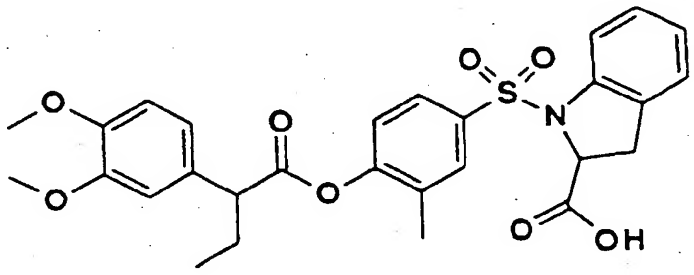


NMR ($CDCl_3$): δ 7.76 (2H, d, J=8.8Hz), 7.57 (1H, d, J=8.0Hz), 7.25-7.02 (5H, m), 6.86-6.85 (3H, m), 4.73 (1H, t, J=8.0Hz), 3.87 (6H, s), 3.59 (1H, t, J=7.8Hz), 3.21-3.17 (2H, brd), 2.24-2.05 (1H, m), 1.97-1.76 (1H, m), 0.97 (3H, t, J=7.6Hz);

TLC : Rf 0.50 (chloroform:methanol:acetic acid=40:2:1).

Example 2(65)

4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(3,4-dimethoxyphenyl)butanoic acid ester

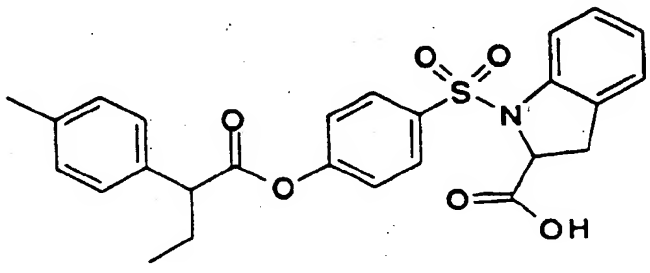


NMR ($DMSO\text{-}d_6$): δ 13.14 (1H, br), 7.80 (1H, s), 7.68 (1H, d-like), 7.35-7.11 (4H, m), 7.02-6.86 (4H, m), 4.97 (1H, dd, J=4.2 and 10.5Hz), 3.79 (1H, t, J=7.4Hz), 3.74 (6H, s), 3.39-2.97 (2H, m), 2.16-1.98 and 1.95-1.72 (each 1H, m), 1.91 (3H, s), 0.89 (3H, t, J=7.2Hz);

TLC : Rf 0.39 (chloroform:methanol:water=8:2:0.2).

Example 2(66)

4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-methylphenyl)butanoic acid ester

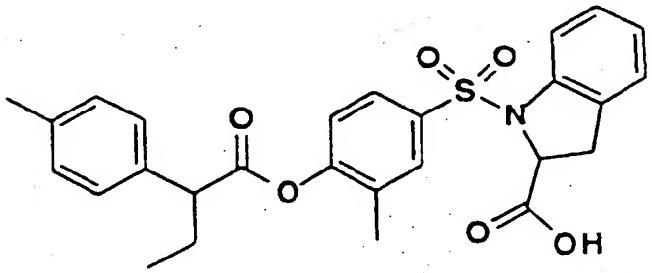


NMR ($CDCl_3$): δ 7.74 (2H, d, J=8.8Hz), 7.58 (1H, d, J=8.0Hz), 7.24-7.02 (9H, m), 4.74 (1H, t, J=8.6Hz), 3.62 (1H,

t, J=7.8Hz), 3.18 (2H, brd), 2.34 (3H, s), 2.27-2.05 (1H, m), 1.97-1.75 (1H, m), 0.96 (3H, t, J=7.4Hz);
TLC : Rf 0.43 (chloroform:methanol:acetic acid=40:2:1).

Example 2(67)

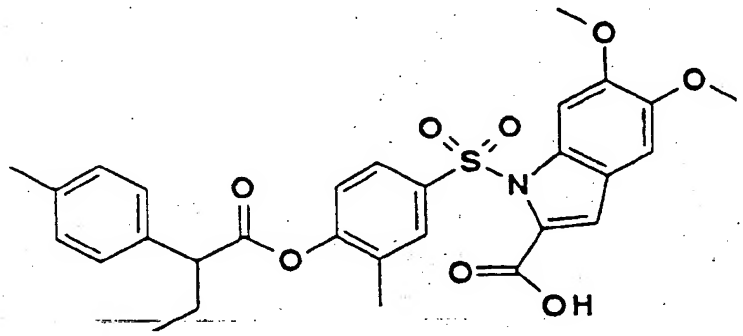
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR (DMSO-d_6):δ 13.08 (1H, br), 7.73 (1H, d, J=2.0Hz), 7.61 (1H, dd, J=2.0 and 8.6Hz), 7.28-6.87 (9H, m), 4.90 (1H, dd, J=4.0 and 10.8Hz), 3.75 (1H, t, J=7.6Hz), 3.32-2.90 (2H, m), 2.22 (3H, s), 2.13-1.91 and 1.86-1.64 (each 1H, m), 1.82 (3H, s), 0.80 (3H, t, J=7.2Hz);
TLC Rf 0.43 (chloroform:methanol:water=8:2:0.2).

Example 2(68)

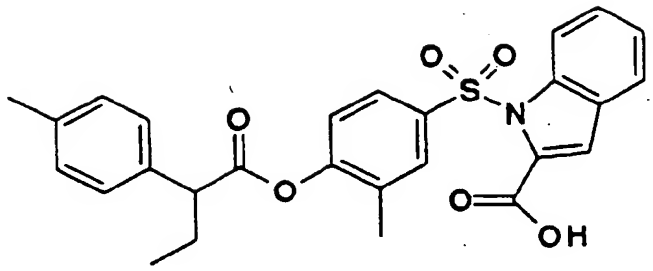
4-(2-carboxy-5,6-dimethoxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.78-7.64 (3H, m), 7.35 (1H, s), 7.23 (2H, d, J=9Hz), 7.15 (2H, d, J=9Hz), 7.00 (1H, d, J=9Hz), 6.95 (1H, s), 4.00 (3H, s), 3.91 (3H, s), 3.85-3.30 (1H, br), 3.65 (1H, t, J=7Hz), 2.33 (3H, s), 2.30-2.10 (1H, m), 2.00-1.80 (1H, m), 1.96 (3H, s), 0.96 (3H, t, J=7Hz);
TLC : Rf 0.23 (ethyl acetate:hexane:acetic acid=5:10:0.5).

Example 2(69)

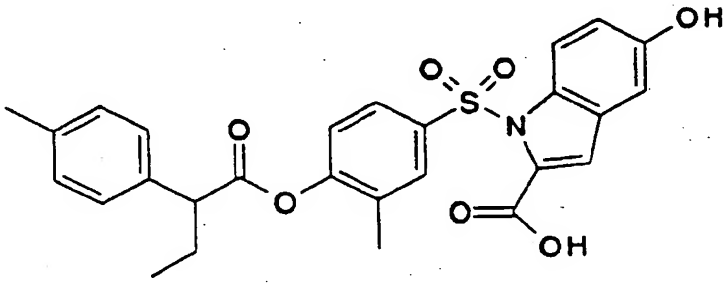
4-(2-carboxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 8.14 (1H, d, J=9Hz), 7.90-7.78 (2H, m), 7.60 (1H, d, J=9Hz), 7.52-7.41 (1H, m), 7.39 (1H, s), 7.35-7.10 (5H, m), 7.03 (1H, d, J=9Hz), 4.00-3.60 (1H, br), 3.66 (1H, t, J=7Hz), 2.33 (3H, s), 2.30-2.07 (1H, m), 2.00-1.75 (1H, m), 1.97 (3H, s), 0.96 (3H, t, J=7Hz);
TLC : Rf 0.28 (ethyl acetate:hexane:acetic acid=5:10:0.5).

Example 2(70)

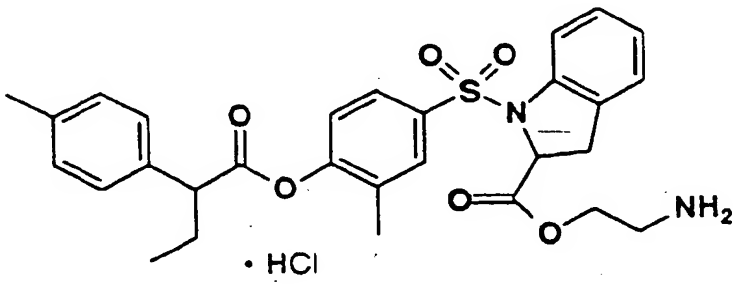
4-(2-carboxy-5-hydroxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.95 (1H, d, J=9Hz), 7.81-7.69 (2H, m), 7.22 (2H, d, J=8Hz), 7.20 (1H, s), 7.15 (2H, d, J=8Hz), 7.00 (1H, d, J=8Hz), 6.97 (1H, dd, J=9,2Hz), 6.89 (1H, d, J=2Hz), 3.80-3.30 (1H, br), 3.66 (1H, t, J=7Hz), 2.33 (3H, s), 2.28-2.10 (1H, m), 2.00-1.80 (1H, m), 1.94 (3H, s), 0.96 (3H, t, J=7Hz);
TLC : Rf 0.24 (ethyl acetate:hexane:acetic acid=10:10:0.5).

Example 2(71)

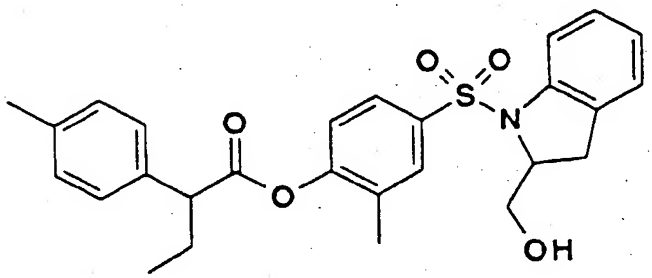
4-(2RS-(2-aminoethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$+CD_3OD): δ 7.8-7.5 (m, 4H), 7.3-7.0 (m, 7H), 5.0-4.8 (m, 1H), 4.6-4.4 (m, 2H), 3.67 (t, J=9.2Hz, 1H), 3.4-3.3 (m, 2H), 3.3-3.2 (m, 2H), 2.34 (s, 3H), 2.3-1.8 (m, 2H), 1.95 (s, 3H), 0.97 (t, J=7.0Hz, 3H);
TLC : Rf 0.5 (chloroform:methanol=4:1).

Example 2(72)

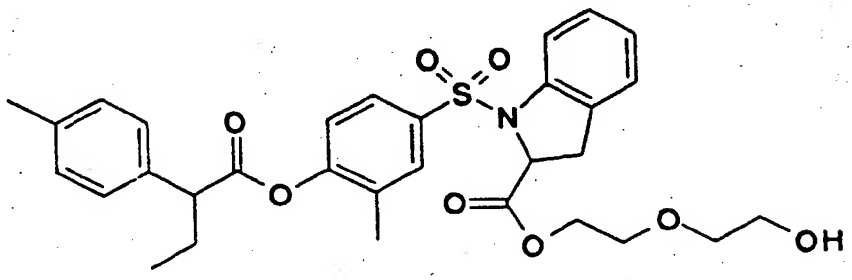
4-(2RS-hydroxymethylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 7.61 (1H, s-like), 7.51-7.40 (2H, m), 7.27-6.96 (8H, m), 5.04 (1H, t-like), 4.34 (1H, m), 3.81 (1H, t, J=7Hz), 3.67-3.57 and 3.48-3.39 (each 1H, m), 2.83-2.68 (2H, m), 2.29 (3H, s), 2.20-1.97 and 1.88-1.67 (each 1H, m), 1.86 (3H, s), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.30 (hexane:ethyl acetate=2:1).

Example 2(73)

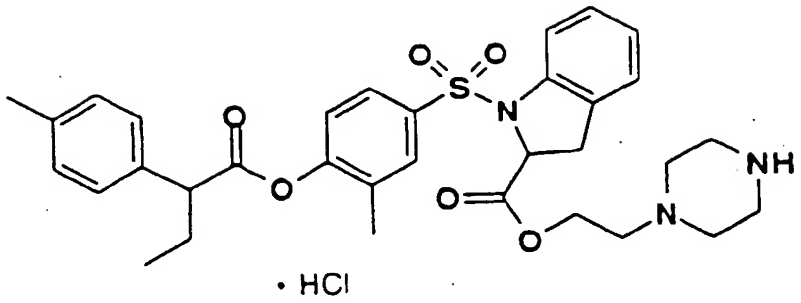
4-(2RS-(2-(2-hydroxyethoxy)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.7-7.5 (m, 3H), 7.3-6.9 (m, 8H), 4.9-4.7 (m, 1H), 4.4-4.3 (m, 2H), 3.8-3.5 (m, 7H), 3.4-3.0 (m, 2H), 2.34 (s, 3H), 2.4-1.8 (m, 2H), 1.93 (s, 3H), 0.97 (t, J=7.2Hz, 3H);
TLC : Rf 0.25 (hexane:ethyl acetate=1:1).

Example 2(74)

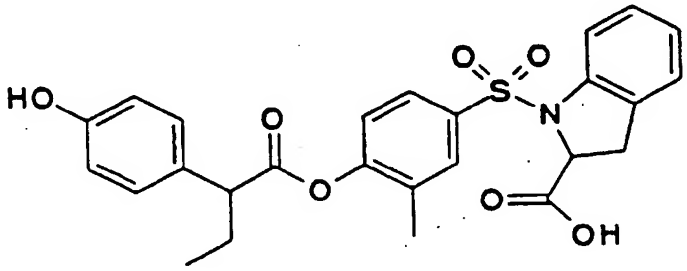
4-(2RS-(2-(piperazin-4-yl)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ 7.7-7.5 (m, 3H), 7.5-7.4 (m, 1H), 7.3-6.9 (m, 7H), 5.2-5.0 (m, 1H), 4.7-4.5 (m, 2H), 4.0-3.5 (m, 11H), 3.4-3.0 (m, 2H), 2.30 (s, 3H), 2.4-2.0 (m, 1H), 1.88 (s, 3H), 2.0-1.8 (m, 1H), 0.93 (t, J=7.2Hz, 3H);
TLC : Rf 0.3 (chloroform:methanol=2:1).

Example 2(75)

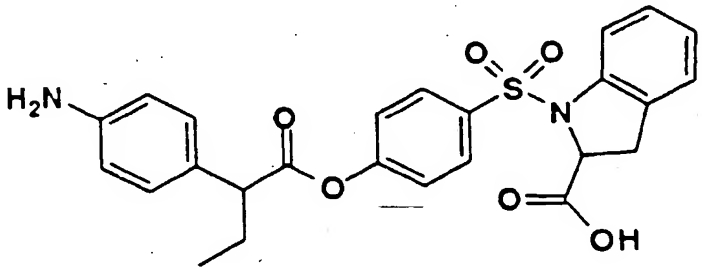
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-hydroxyphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.7-7.5 (3H ,m), 7.3-7.1 (3H, m), 7.1-6.9 (3H, m), 6.80 (2H, d, J=8.4Hz), 4.8-4.7 (1H, m), 3.7-3.3 (1H, m), 3.3-3.1 (2H, m), 2.3-2.0 (1H, m), 2.0-1.8 (1H,m), 1.91 (3H, s), 0.96 (3H, t, J=7.4Hz);
TLC : Rf 0.42 (chloroform;methanol:water=8:2:0.2).

Example 2(76)

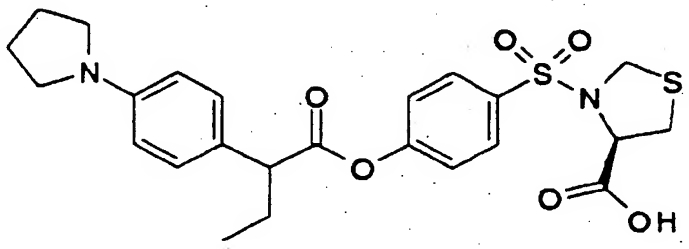
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-aminophenyl)butanoic acid ester



NMR ($DMSO-d_6$): δ 7.83 (2H, d, J=8.4Hz), 7.30 (1H, d, J=8.2Hz), 7.12 (2H, d, J=8.4Hz), 6.97 (2H, d, J=8.4Hz), 7.17-6.90 (3H, m), 6.53 (2H, d, J=8.4Hz), 4.80-4.73 (1H, m), 3.54 (1H, t, J=7.6Hz), 3.25-2.93 (2H, m), 2.09-1.90 (1H, m), 1.78-1.60 (1H, m), 0.86 (3H, t, J=7.2Hz);
TLC : Rf 0.20 (chloroform:methanol:acetic acid=40:2:1).

Example 2(77)

4-(4S-carboxyperhydrothiazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

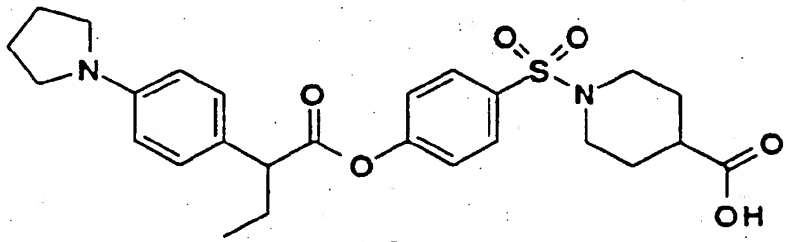


· HCl

NMR ($CDCl_3$): δ 7.85 (2H, d, J=8.8Hz), 7.21 (2H, d, J=8.8Hz), 7.17 (2H, d, J=8.8Hz), 6.57 (2H, d, J=8.8Hz), 4.83 (1H, dd, J=7.0 and 3.4Hz), 4.67 (1H, d, J=9.0Hz), 4.40 (1H, d, J=9.0Hz), 3.59 (1H, t, J=7.6Hz), 3.40-3.18 (5H, m), 3.01 (1H, dd, J=11.4 and 7.0Hz), 2.30-2.05 and 2.05-1.75 (each 1H, m), 2.10-1.95 (4H, m), 0.98 (3H, t, J=7.6Hz);
TLC : Rf 0.36 (acetic acid:methanol:chloroform=1:2:40).

Example 2(78)

4-(4-carboxypiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

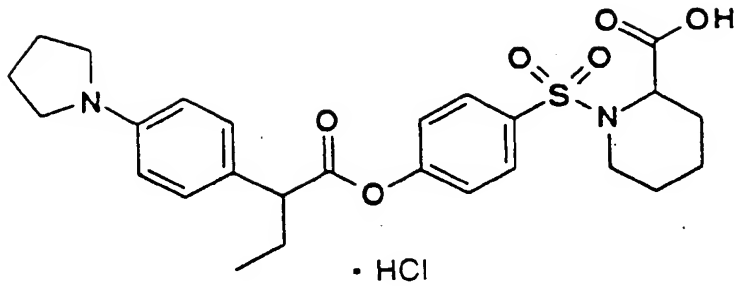


· HCl

NMR ($CDCl_3$): δ 7.71 (2H, d, J=8.8Hz), 7.21 (2H, d, J=8.8Hz), 7.17 (2H, d, J=8.8Hz), 6.55 (2H, d, J=8.8Hz), 3.72-3.54 (2H, m), 3.59 (1H, t, J=7.6Hz), 3.36-3.20 (4H, m), 2.45 (2H, t-like) 2.38-1.70 (7H, m), 2.08-1.94 (4H, m), 0.98 (3H, t, J=7.4Hz);
TLC : Rf 0.34 (acetic acid:methanol:chloroform=1:2:40).

Example 2(79)

4-(2RS-carboxypiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

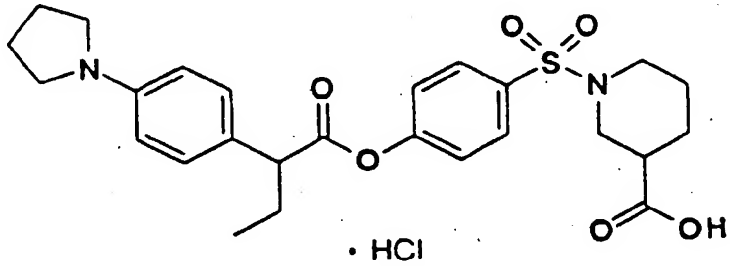


• HCl

NMR ($CDCl_3$): δ 7.75 (2H, d, J=8.8Hz), 7.21 (2H, d, J=8.8Hz), 7.08 (2H, d, J=8.8Hz), 6.55 (2H, d, J=8.8Hz), 4.8-4.7 (1H, m), 3.8-3.7 (1H, m), 3.58 (1H, t, J=7.5Hz), 3.4-3.1 (5H, m), 2.3-1.2 (12H, m), 0.97 (3H, t, J=7.4Hz);
TLC : Rf 0.48 (acetic acid:methanol:chloroform=1:2:50).

Example 2(80)

4-(3RS-carboxypiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

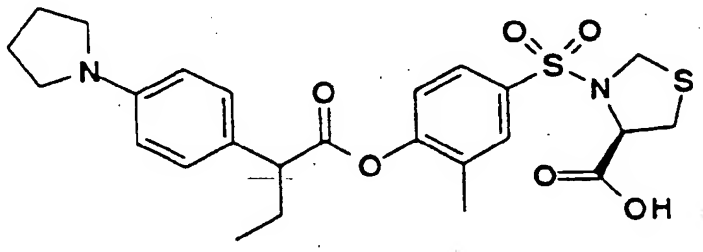


• HCl

NMR ($CDCl_3$): δ 7.75 (2H, d, J=8.4Hz), 7.7-7.3 (4H, m), 7.19 (2H, d, J=8.4Hz), 4.0-3.4 (8H, m), 2.7-2.5 (2H, m), 2.5-2.1 (5H, m), 2.1-1.3 (5H, m), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.32 (acetic acid:methanol:chloroform=1:2:100).

Example 2(81)

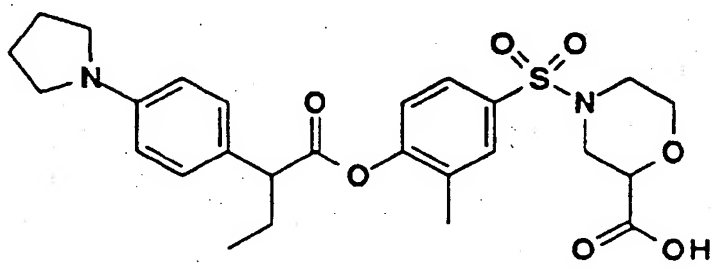
4-(4S-carboxyperhydrothiazol-3-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$+CD_3OD): δ 7.69 (1H, s), 7.66 (1H, d, J=8.0Hz), 7.21 (2H, d, J=8.6Hz), 7.07 (1H, d, J=8.0Hz), 6.55 (2H, d, J=8.6Hz), 4.71 (1H, dd, J=7.2, 3.2Hz), 4.63 (1H, d, J=9.8Hz), 4.45 (1H, d, J=9.8Hz), 3.61 (1H, t, J=7.7Hz), 3.4-3.2 (5H, m), 2.84 (1H, dd, J=11.2, 7.2Hz), 2.3-2.1 (1H, m), 2.1-1.8 (4H, br), 2.02 (3H, s), 0.98 (3H, d, J=7.3Hz);
TLC : Rf 0.55 (chloroform:methanol:acetic acid=25:5:1).

Example 2(82)

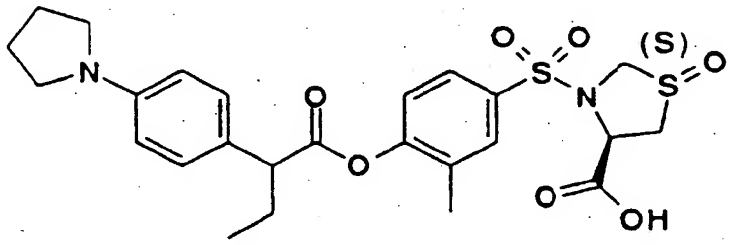
4-(2RS-carboxymorpholin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (CD_3OD): δ 7.65-7.54 (2H, m), 7.20 (2H, d, J=8Hz), 7.15 (1H, d, J=8Hz), 6.58 (2H, d, J=8Hz), 4.03-3.80 (3H, m), 3.71-3.38 (3H, m), 3.37-3.15 (4H, m), 2.50-1.78 (11H, m), 0.97 (3H, t, J=7Hz);
TLC : Rf 0.25 (methanol:chloroform=3:17).

Example 2(83)

4-(1S-oxo-4S-carboxyperhydrothiazol-3-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

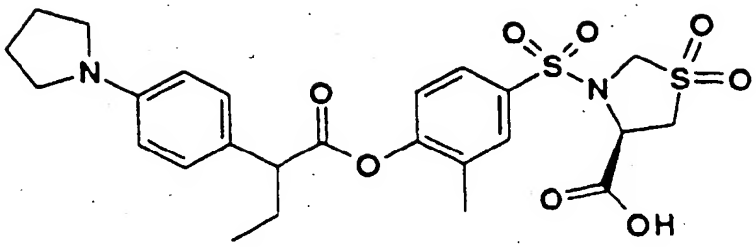


· HCl

NMR (CD_3OD): δ 7.90.7.75 (2H, m), 7.61 (4H, s), 7.18 (1H, d, J=8.5Hz), 5.25 (1H, dd, J=8.5, 2.0Hz), 5.19 (1H, d, J=12.0Hz), 4.13 (1H, d, J=12.0Hz), 3.98 (1H, t, J=7.5Hz), 3.85-3.70 (4H, m), 3.41 (1H, dd, J=14.5, 2.0Hz), 3.03 (1H, dd, J=14.5, 8.5Hz), 2.35-2.20 (4H, m), 2.40-1.80 (2H, m), 2.04 (3H, s), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.18 (chloroform:methanol:acetic acid=40:10:1).

Example 2(84)

4-(4S-carboxy-1,1-dioxoperhydrothiazol-3-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

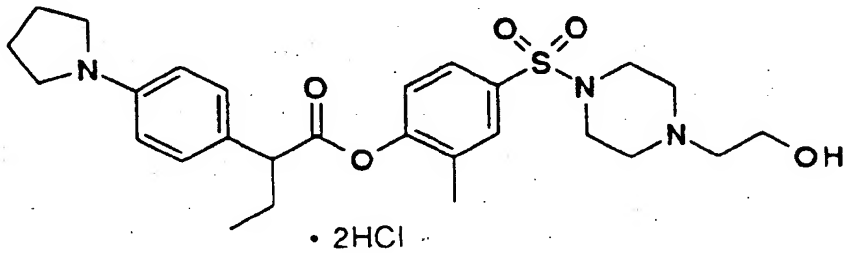


• HCl

NMR ($CDCl_3$): δ 7.75-7.65 (2H, m), 7.48 (4H, s), 7.10 (1H, d, J=8.5Hz), 5.06 (1H, dd, J=8.5, 4.0Hz), 4.68 (1H, d, J=11.0Hz), 4.26 (1H, d, J=11.0Hz), 3.78 (1H, t, J=7.5Hz), 3.70-3.55 (4H, m), 3.55-3.35 (2H, m), 2.40-2.25 (4H, m), 2.40-1.80 (2H, m), 2.07 (3H, s), 1.01 (3H, t, J=7.5Hz);
TLC : Rf 0.14 (chloroform:methanol:acetic:acid=40:10:1).

Example 2(85)

4-(4-(2-hydroxyethyl)piperazin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

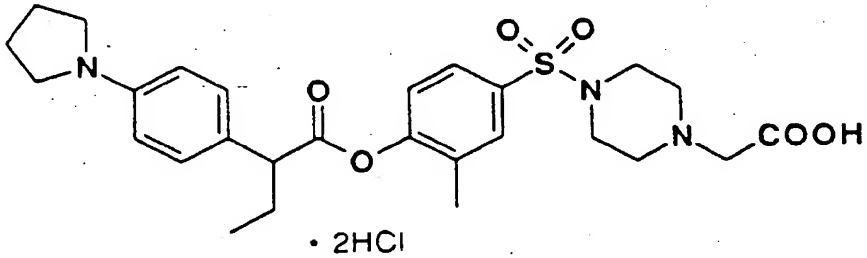


• 2HCl

NMR (CD_3OD): δ 7.75-7.47 (6H, m), 7.23 (1H, d, J=8.8Hz), 4.03-3.79 (5H, m), 3.79-3.57 (6H, m), 3.40-3.14 (4H, m), 2.77 (2H, t-like, J=13.8Hz), 2.38-2.15 (5H, m), 2.06 (3H, s), 2.15-1.84 (1H, m), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.21 (hexane:ethyl acetate=1:1).

Example 2(86)

4-(4-carboxymethylpiperazin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



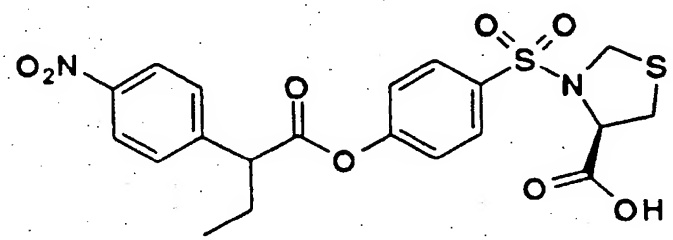
• 2HCl

NMR (CD_3OD): δ 7.79-7.53 (6H, m), 7.24 (1H, d, J=8.0Hz), 4.14 (2H, s), 4.00 (1H, t, J=7.8Hz), 3.87-3.70 (4H, m), 3.52 (8H, brs), 2.44-2.15 (5H, m), 2.07 (3H, s), 2.15-1.82 (1H, m), 1.00 (3H, t, J=7.2Hz);

TLC : Rf 0.63 (chloroform:methanol:acetic acid=15:2:1).

Example 2(87)

4-(4S-carboxyperhydrothiazol-3-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester

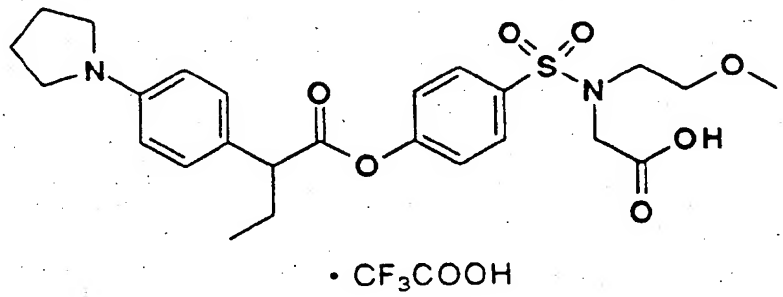


NMR ($CDCl_3$): δ 8.27 (2H, d, J=8.8Hz), 7.94 (2H, d, J=8.8Hz), 7.68 (2H, d, J=8.8Hz), 7.26 (2H, d, J=8.8Hz), 4.86 (1H, dd, J=3.6 and 7.4Hz), 4.73 (1H, d, J=8.0Hz), 4.41 (1H, d, J=8.0Hz), 4.03 (1H, t, J=7.6Hz), 3.17 (1H, dd, J=11.5 and 3.6Hz), 2.93 (1H, dd, J=11.5 and 7.4Hz), 2.40-2.15 and 2.10-1.85 (each 1H, m), 1.00 (3H, t, J=7.2Hz);

TLC : Rf 0.38 (acetic acid:methanol:chloroform=1:2:40).

Example 2(88)

4-(N-carboxymethyl-N-2-methoxyethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · trifluoroacetate



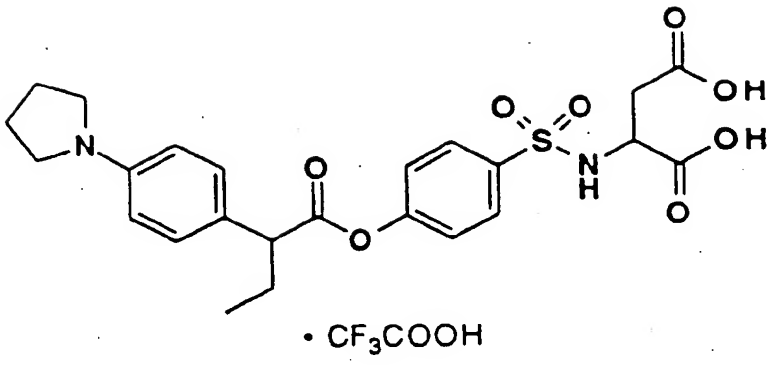
$\cdot CF_3COOH$

NMR (CD_3OD): δ 7.85 (2H, d, J=8.6Hz), 7.41 (2H, d, J=8.6Hz), 7.17 (2H, d, J=8.6Hz), 7.11 (2H, d, J=8.6Hz), 4.10 (2H, s), 3.77 (1H, t, J=6.0Hz), 3.46 (8H, m), 3.20 (3H, s), 2.20 (1H, m), 2.15 (4H, m), 1.90 (1H, m), 0.97 (3H, t, J=7.0Hz);

TLC : Rf 0.32 (chloroform:methanol:water=9:1:0.1).

Example 2(89)

4-(N-1RS,2-dicarboxyethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · trifluoroacetate

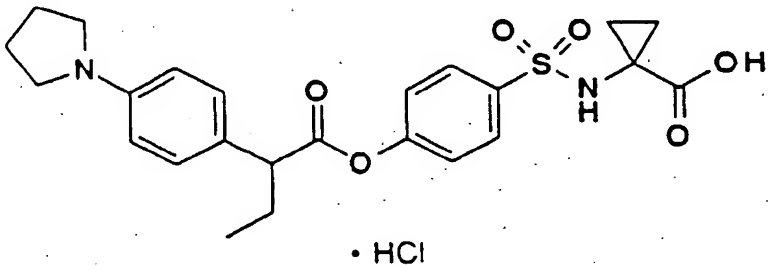


NMR (CD_3OD): δ 7.87 (2H, d, J=8.6Hz), 7.36 (2H, brd, J=8.6Hz), 7.14 (2H, d, J=8.6Hz), 7.00 (2H, brd, J=8.6Hz), 4.21 (1H, t, J=6.0Hz), 3.74 (1H, m), 3.48 (4H, m), 2.72 (2H, d, J=6.2Hz), 2.18 (1H, m), 2.13 (4H, m), 1.87 (1H, m), 0.97 (3H, t, J=7.4Hz);

TLC : Rf 0.26 (chloroform:methanol:water=9:1:0.1).

Example 2(90)

4-(N-(1-carboxycydobutane)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

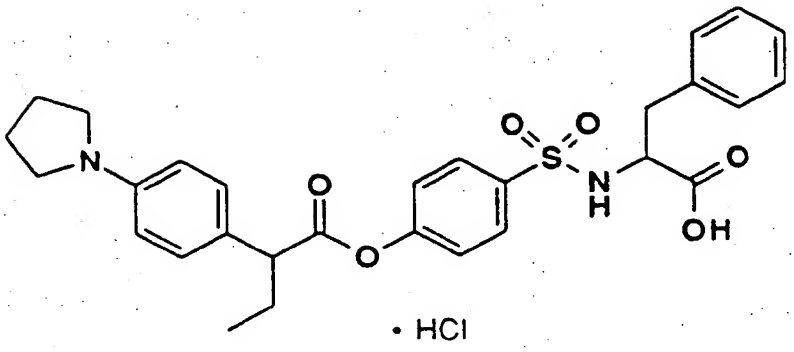


NMR ($CDCl_3$): δ 7.81 (2H, d, J=8.8Hz), 7.15 (2H, d, J=8.8Hz), 7.05 (2H, d, J=8.8Hz), 6.55 (2H, d, J=8.8Hz), 5.66 (1H, s), 3.58 (1H, t, J=7.6Hz), 3.36-3.18 (4H, t-like), 2.30-2.00 and 2.00-1.75 (each 1H, m), 2.06-1.96 (4H, m), 1.56-1.35 (4H, m), 0.97 (3H, t, J=7.4Hz);

TLC : Rf 0.38 (acetic acid:methanol:chloroform=1:2:40).

Example 2(91)

4-(N-1RS-carboxy-2-phenylethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

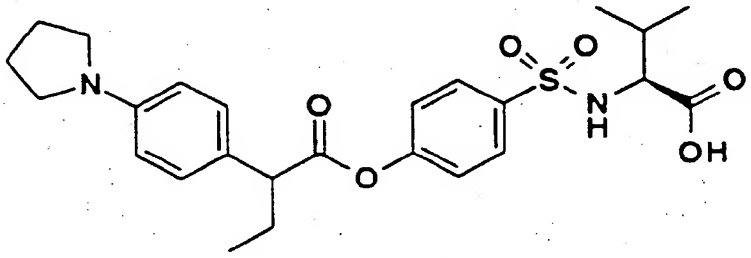


• HCl

NMR (DMSO-d_6): δ 8.38 (1H, d, J=10Hz), 7.55 (2H, d, J=9Hz), 7.30-7.00 (9H, m), 6.76 (2H, d, J=9Hz), 3.95-3.79 (1H, m), 3.71 (1H, t, J=7Hz), 3.40-3.20 (4H, m), 2.94 (1H, dd, J=15Hz, 5Hz), 2.70 (1H, dd, J=15Hz, 8Hz), 2.20-1.90 (5H, m), 1.90-1.65 (1H, m), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.19 (ethyl acetate:hexane:acetic acid=5:5:0.1).

Example 2(92)

4-(N-1S-carboxy-2-methylpropylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

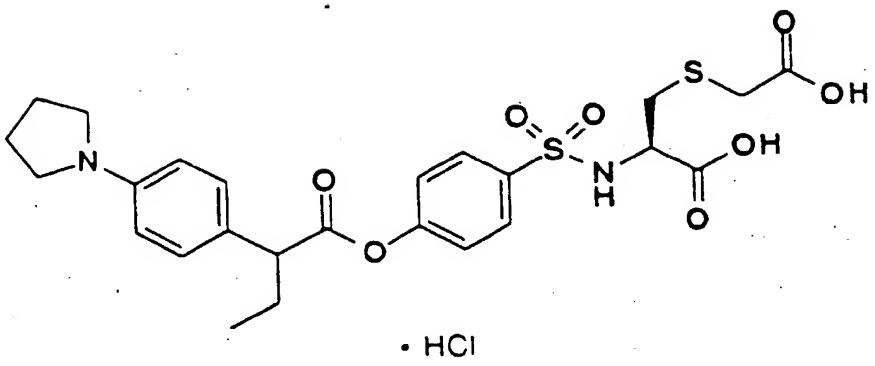


• HCl

NMR (DMSO-d_6): δ 8.05 (1H, d, J=9Hz), 7.78 (2H, d, J=8Hz), 7.25 (2H, d, J=8Hz), 7.17 (2H, d, J=8Hz), 6.86-6.70 (2H, m), 3.73 (1H, t, J=7Hz), 3.50 (1H, dd, J=9Hz, 6Hz), 3.38-3.20 (4H, m), 2.20-1.68 (7H, m), 0.88 (3H, t, J=7Hz), 0.80 (3H, d, J=7Hz), 0.76 (3H, d, J=7Hz);
TLC : Rf 0.34 (ethyl acetate).

Example 2(93)

4-(N-(1S-carboxy-2-carboxymethylthioethyl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

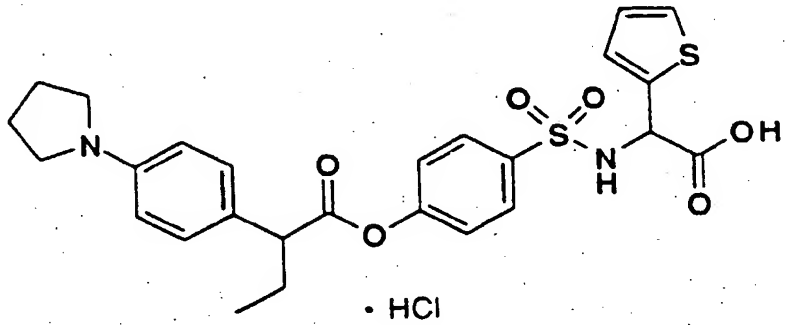


• HCl

NMR (CD_3OD): δ 7.89 (2H, d, J=8.8Hz), 7.63 (2H, d, J=15.0Hz), 7.62 (2H, d, J=15.0Hz), 7.18 (2H, d, J=8.8Hz), 4.08 (1 H, dd, J=5.9, 7.5Hz), 3.91 (1H, t, J=7.5Hz), 3.82-3.70 (4H, m), 3.19 (2H, s), 3.00 (1H, dd, J=5.9, 14.0Hz), 2.84 (1H, dd, J=7.5, 14.0Hz), 2.40-2.12 (5H, m), 2.02-1.80 (1H, m), 0.98 (3H, t, J=7.0Hz);
TLC : Rf 0.20 (chloroform:methanol:water=7:3:0.3).

Example 2(94)

4-(N-1RS-carboxy-1-(thiophen-2-yl)methylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

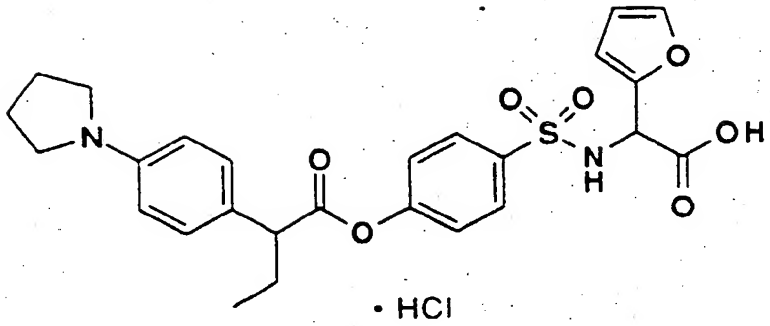


• HCl

NMR ($DMSO-d_6$): δ 8.88 (1H, d, J=9.0Hz), 7.77 (2H, d, J=8.8Hz), 7.40 (1H, dd, J=1.2, 5.0Hz), 7.24 (2H, d, J=8.4Hz), 7.14 (2H, d, J=8.8Hz), 7.00-6.91 (1H, m), 6.88 (1H, dd, J=3.7, 5.0Hz), 6.85-6.72 (2H, m), 5.16 (1H, d, J=9.0Hz), 3.71 (1H, t, J=7.2Hz), 3.40-3.20 (4H, m), 2.20-1.90 (5H, m), 1.88-1.70 (1H, m), 0.89 (3H, t, J=7.2Hz);
TLC : Rf 0.27 (chloroform:methanoi:water=4:1:0.1).

Example 2(95)

4-(N-1RS-carboxy-1-(furan-2-yl)methylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



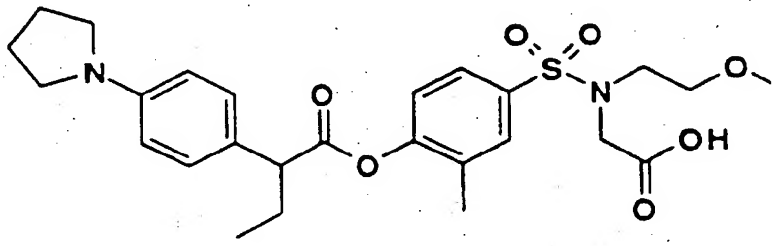
• HCl

NMR (DMSO-d_6): δ 8.78 (1H, d, J=9.0Hz), 7.75 (2H, d, J=8.6Hz), 7.46 (1H, m), 7.24 (2H, d, J=8.2Hz), 7.12 (2H, d J=8.6Hz), 6.90-6.70 (2H, m), 6.31-6.24 (1H, m), 6.19 (1H, d, J=2.8Hz), 5.02 (1H, d, J=9.0Hz), 3.71 (1H, t, J=7.6Hz), 3 40-3 20 (4H, m), 2.20-1.86 (5H, m), 1.86-1.68 (1H, m), 0.89 (3H, t, J=7.4Hz);

TLC : Rf 0.27 (chloroform:methanol:water=4:1:0.1).

Example 2(96)

4-(N-carboxymethyl-N-2-methoxyethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

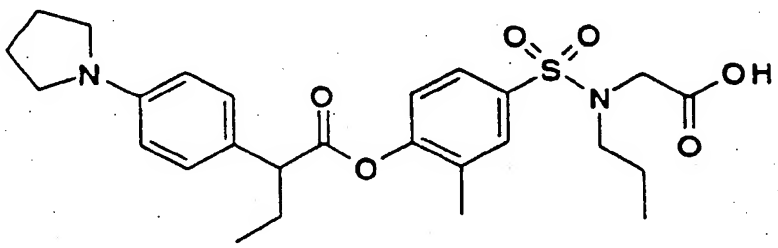


NMR ($CDCl_3$): δ 7.64 (1H, d, J=2.0Hz), 7.61 (1H, dd, J=8.0, 2.0Hz), 7.21 (2H, d, J=8.5Hz), 7.04 (1H, d, J=8.0Hz), 6.55 (2H, d, J=8.5Hz), 4.08 (2H, s), 3.61 (1H, t, J=7.5Hz), 3.55 (2H, t, J=4.5Hz), 3.40 (2H, t, J=4.5Hz), 3.35-3.20 (4H, m), 3.29 (3H, s), 2.30-1.70 (2H, m), 2.05-1.95 (4H, m), 2.01 (3H, s), 0.99 (3H, t, J=7.5Hz);

TLC : Rf 0.47 (chloroform:methanol:acetic acid=40:2:1).

Example 2(97)

4-(N-propyl-N-carboxymethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

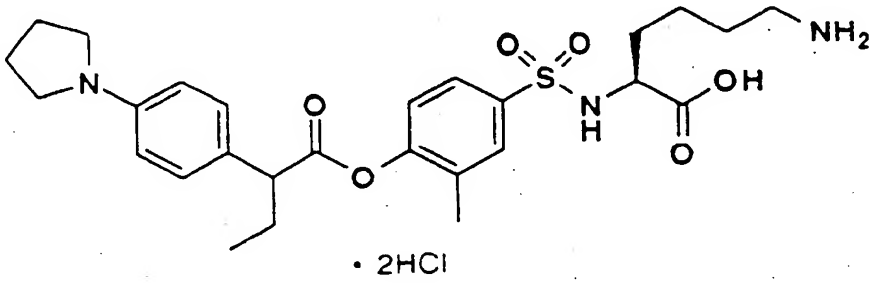


NMR ($CDCl_3$): δ 7.70-7.55 (2H, m), 7.23 (2H, d, J=8Hz), 7.01 (1H, d, J=8Hz), 6.55 (2H, d, J=8Hz), 4.20-3.80 (1H,

br), 3.98 (2H, s), 3.60 (1H, t, J=7Hz), 3.35-3.07 (6H, m), 2.28-1.75 (9H, m), 1.60-1.38 (2H, m), 0.98 (3H, t, J=7Hz), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.23 (chloroform:methanol=19:1).

Example 2(98)

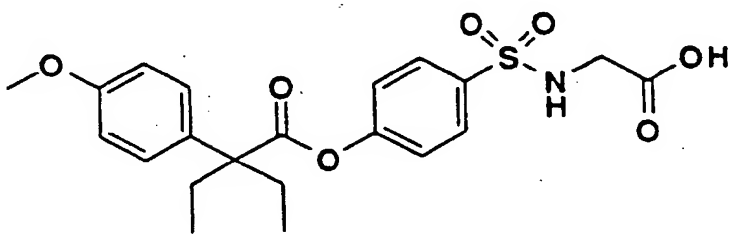
4-(N-1S-carboxy-5-aminopentylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (CD_3OD): δ 7.80-7.47 (6H, m), 7.10 (1H, d, J=8Hz), 3.95 (1H, t, J=7Hz), 3.90-3.68 (5H, m), 2.95-2.80 (2H, m), 2.35-2.20 (5H, m), 2.10-1.85 (1H, m), 1.99 (3H, s), 1.85-1.30 (6H, m), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.22 (chloroform:methanol:water=8:2:0.1).

Example 2(99)

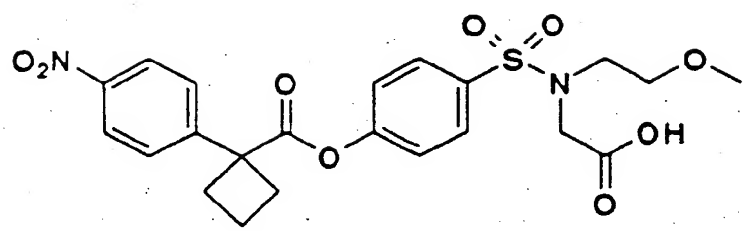
4-(N-carboxymethylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester



NMR ($CDCl_3$): δ 7.80 (2H, d, J=8.8Hz), 7.25 (2H, d, J=8.8Hz), 7.04 (2H, d, J=8.6Hz), 6.90 (2H, d, J=8.8Hz), 3.80 (3H, s), 3.73 (2H, brs), 2.25-2.00 (4H, m), 0.82 (6H, t, J=7.4Hz);
TLC : Rf 0.10 (hexane:ethyl acetate=2:1).

Example 2(100)

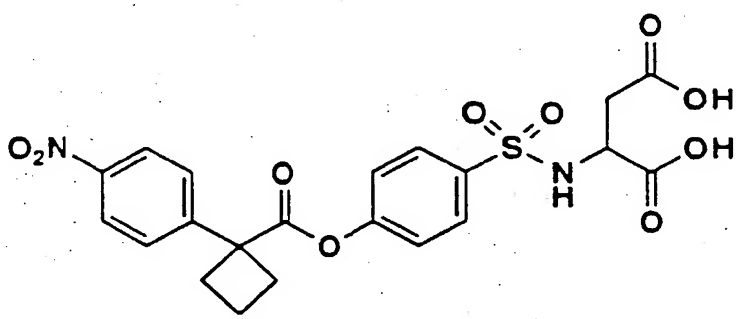
4-(N-2-methoxyethyl-N-carboxymethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR ($CDCl_3$): δ 8.25 (2H, d, J=9.0Hz), 7.82 (2H, d, J=9.0Hz), 7.55 (2H, d, J=9.0Hz), 7,11 (2H, d, J=9.0Hz), 4,13 (2H, s), 3.53 (2H, t, J=5.0Hz), 3.41 (2H, t, J=5.0Hz), 3.27 (3H, s), 3.06 (2H, m), 2.67 (2H, m), 2.26 (1H, m), 2.04 (1H, m);
TLC : Rf 0.29 (chloroform:methanol:water=9:1:0.1).

Example 2(101)

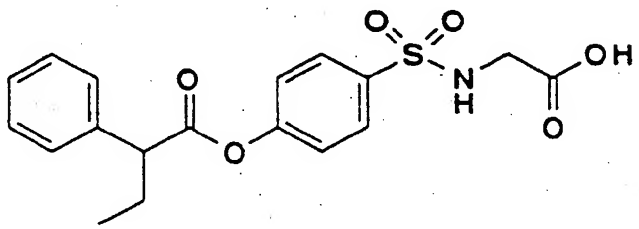
4-(N-1RS,2-dicarboxyethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (CD_3OD): δ 8.27 (2H, d, J=8.8Hz), 7.87 (2H, d, J=8.8Hz), 7.65 (2H, d, J=8.8Hz), 7.15 (2H, d, J=8.8Hz), 4.21 (1H, t, J=5.8Hz), 3.05 (2H, m), 2.71 (4H, m), 2.25 (1H, m), 2.04 (1H, m);
TLC : Rf 0.17 (chloroform:methanol:water=8:2:0.2).

Example 2(102)

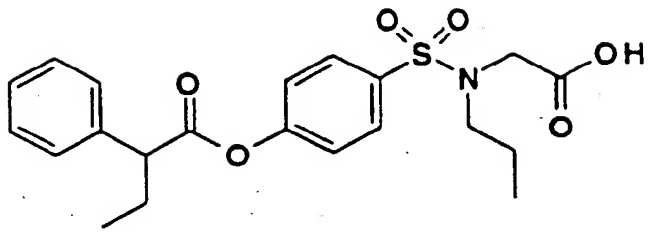
4-(N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR (DMSO-d_6): δ 8.04 (1H, brs), 7.82 (2H, d, J=8Hz), 7.45-7.25 (5H, m), 7.21 (2H, d, J=8Hz), 3.86 (1H, t, J=7Hz), 3.56 (2H, s), 2.10 and 1.85(each 1H, m), 0.91 (3H, t, J=7Hz);
TLC : Rf 0.32 (acetic acid:methanol:chloroform=1:3:30).

Example 2(103)

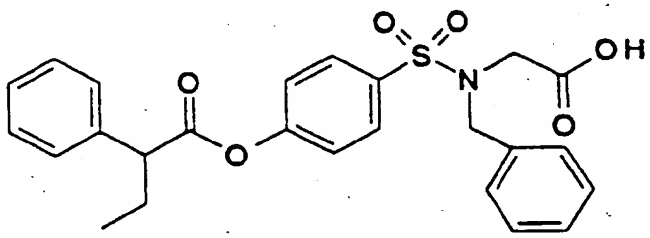
4-(N-propyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR (DMSO-d_6): δ 12.65 (1H, brs), 8.04 (1H, brs), 7.84 (2H, d, J=8Hz), 7.45-7.25 (5H, m), 7.21 (2H, d, J=8Hz), 3.92 (2H, s), 3.85 (1H, t, J=7Hz), 3.10 (2H, t), 2.10 and 1.86 (each 1H, m), 1.44 (2H, m), 0.92 (3H, t, J=7Hz), 0.77 (3H, t, J=7Hz);
TLC : Rf 0.54 (acetic acid:methanol:chloroform=1:3:30).

Example 2(104)

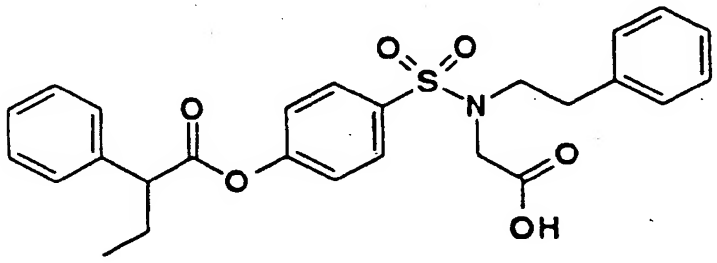
4-(N-benzyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.90-7.79 (2H, m), 7.43-7.08 (12H, m), 6.34 (1H, br), 4.46 (2H, s), 3.90 (2H, s), 3.70 (1H, t, J=7Hz), 2.22 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.92 (1H, ddq, J=14Hz, 7Hz, 7Hz), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.42 (dichloromethane:methanol=9:1).

Example 2(105)

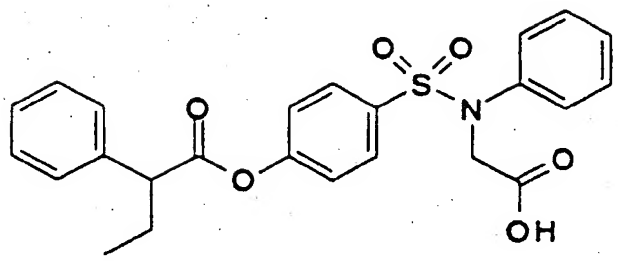
4-(N-2-phenylethyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.77 (2H, d, J=8Hz), 7.40.7.04 (12H, m), 5.89 (1H, br), 3.95 (2H, s), 3.69 (1H, t, J=7Hz), 3.53-3.40 (2H, m), 2.91-2.80 (2H, m), 2.21 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.90 (1H, ddq, J=14Hz, 7Hz, 7hz), 0.97 (3H, t, J=7Hz);
TLC : Rf 0.41 (dichloromethane:methanol=9:1).

Example 2(106)

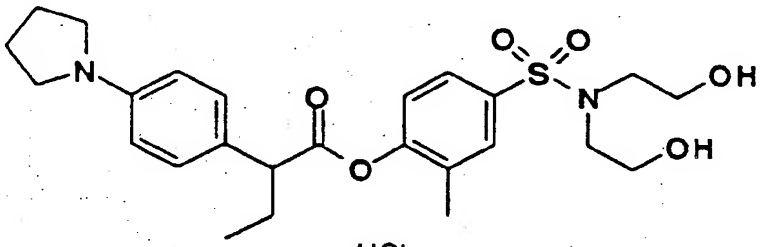
4-(N-phenyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.63 (2H, d, J=8Hz), 7.45-7.04 (12H, m), 6.20 (1H, br), 4.40 (2H, s), 3.70 (1H, t, J=7Hz), 2.23 (1H, ddq, J=14Hz, 7Hz, 7hz), 1.91 (1H, ddq, J=14Hz, 7Hz, 7Hz), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.41 (dichloromethane:methanol=9:1).

Example 2(107)

4-(N,N-bis(2-hydroxyethyl)sulfamoyl)-2-methyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

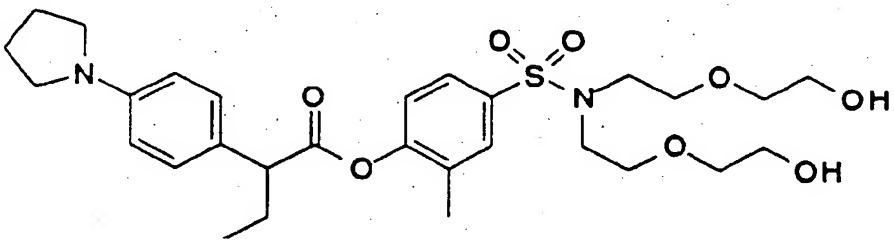


• HCl

NMR (CD_3OD): δ 7.78-7.50 (6H, m), 7.15 (1H, d, J=8Hz), 3.96 (1H, t, J=7Hz), 3.95-3.80 (8H, m), 3.35-3.18 (4H, m), 2.40-2.15 (5H, m), 2.10-1.80 (1H, m), 2.02 (3H, s), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.23 (hexane:ethyl acetate=1:1).

Example 2(108)

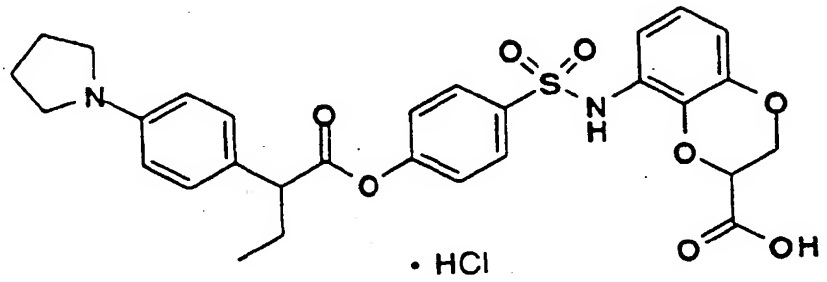
4-(N,N-bis(2-(2-hydroxyethoxy)ethyl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70-7.55 (2H, m), 7.23 (2H, d, J=9Hz), 7.06 (1H, d, J=8Hz), 6.55 (2H, d, J=9Hz), 3.75-3.45 (13H, m), 3.43-3.23 (8H, m), 3.05 (2H, brs), 2.30-1.73 (9H, m), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.33 (ethyl acetate).

Example 2(109)

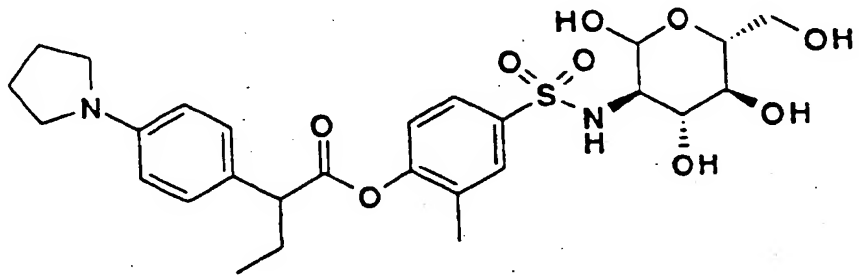
4-(N-(3RS-carboxy-1,4-benzodioxan-5-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 9.67 (1H, s), 7.80 (2H, d, J=9Hz), 7.20 (2H, d, J=9Hz), 7.13 (2H, d, J=9Hz), 6.84-6.57 (5H, m), 4.78 (1H, t, J=3Hz), 4.28 (1H, dd, J=11Hz, 3Hz), 4.13-4.00 (1H, m), 3.68 (1H, t, J=7Hz), 3.35-3.18 (4H, m), 2.15-1.88 (5H, ml, 1.88-1.60 (1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.18 (chloroform:methanol:acetic acid=40:2:1).

Example 2(110)

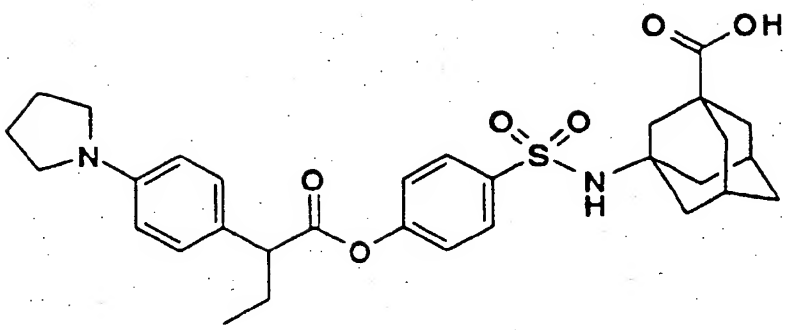
4-(N-2RS-hydroxy-4R-hydroxy-5R-hydroxy-6R-hydroxymethylperhydropyran-3R-ylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (DMSO-d_6+3 drop of CD_3OD): δ 7.80-7.60 (2H, m), 7.20 (2H, d, J=8.5Hz), 7.05 (1H, d, J=8.5Hz), 6.60 (2H, d, J=8.5Hz), 4.78 (1H, d, J=3.5Hz), 3.70 (1H, t, J=7.5Hz), 3.65-3.35 (4H, m), 3.30-3.15 (4H, m), 3.03 (1H, t, J=9.0Hz), 2.90 (1H, dd, J=10.5, 3.5Hz), 2.20-1.60 (2H, m), 2.00-1.90 (4H, m), 1.94 (3H, s), 0.91 (3H, t, J=7.5Hz);
TLC : Rf 0.55 (chloroform:methanol:water=40:10:1).

Example 2(111)

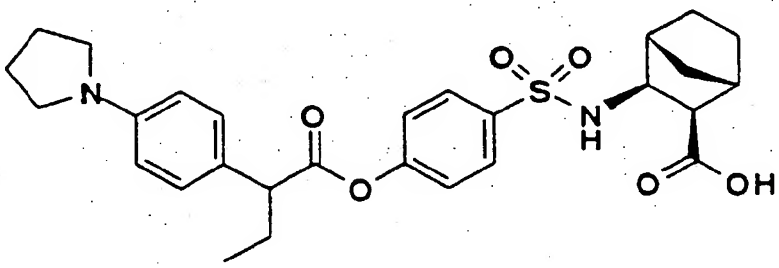
4-(N-3-carboxyadamantan-1-ylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.85 (2H, d, J=8.8Hz), 7.22 (2H, d, J=8.8Hz), 7.12 (2H, d, J=8.8Hz), 6.54 (2H, d, J=8.8Hz), 4.60 (1H, s), 3.59 (1H, t, J=7.4Hz), 3.40-3.15 (4H, m), 2.30-1.40 (20H, m), 0.98 (3H, t, J=7.6Hz);
TLC : Rf 0.60 (chloroform:methanol:acetic acid=40:2:1).

Example 2(112)

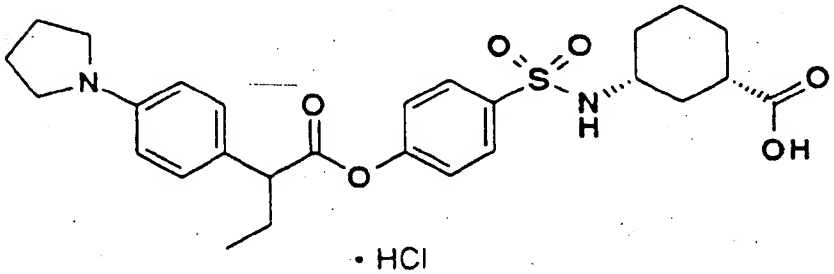
4-(N-(1S,4R,3R-carboxybicyclo[2.2.1]heptan-2S-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.83 (2H, d, J=8.6Hz), 7.21 (2H, d, J=8.6Hz), 7.11 (2H, d, J=8.6Hz), 6.55 (2H, d, J=8.6Hz), 7.6-7.4 (1H, br), 3.58 (1H, t, J=7.6Hz), 3.58 (1H, t, J=8.0Hz), 3.40-3.20 (4H, m), 2.64 (1H, d, J=8.0Hz), 2.42 (1H, s), 2.30-1.70 (4H, m), 2.10-1.90 (4H, m), 1.50-1.30 (2H, m), 1.30-0.90 (3H, m), 0.97 (3H, t, J=7.3Hz);
TLC : Rf 0.33 (chloroform:methanol:acetic acid=40:2:1).

Example 2(113)

4-(N-3S-carboxycydohexane-1R-ylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



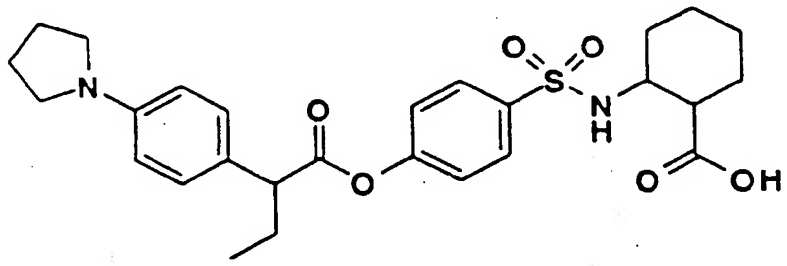
• HCl

NMR (DMSO-d_6): δ 7.90-7.70 (3H, m), 7.30-7.10 (4H, m), 6.70 (2H, d, J=9Hz), 3.71 (1H, t, J=7Hz), 3.35-3.15 (4H, m), 3.09-2.86 (1H, m), 2.27-1.45 (11H, m), 1.33-0.95 (4H, m), 0.89 (3H, t, J=7Hz);

TLC : Rf 0.36 (ethyl acetate:hexane:acetic acid=5:5:0.1).

Example 2(114)

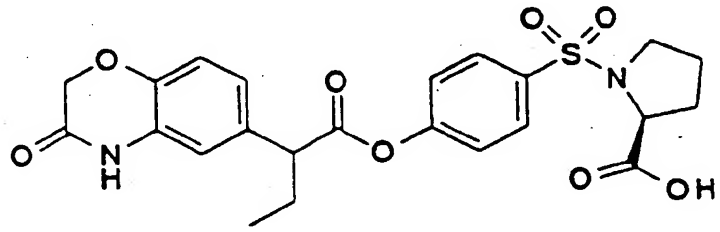
4-(N-2RS-carboxycyclohexane-1RS-ylsulfamoylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.84 (2H, d, J=8.8Hz), 7.23-7.08 (4H, m), 6.55 (2H, d, J=8.6Hz), 5.70 (1H, brs), 3.59 (1H, t, J=8.0Hz), 3.45 (1H, brs), 3.32-3.26 (4H, m), 2.65 (1H, brs), 2.25-1.20 (14H, m), 0.98 (3H, t, J=7.0Hz);
TLC : Rf 0.22 (hexane:ethyl acetate=1:1).

Example 2(115)

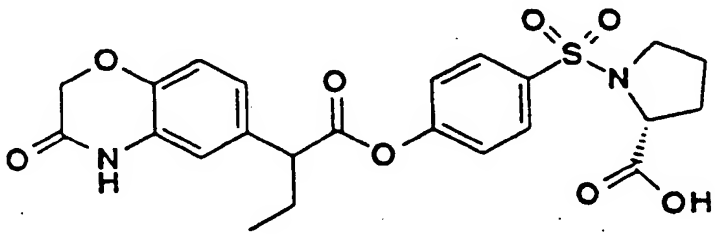
4-(2S-carboxypyrrolidin-1-ylsultonyl)phenyl 2RS-(2H-1,4-benzoxazin-3-on-6-yl)butanoic acid ester



NMR (DMSO-d_6): δ 10.73 (1H, s), 7.88 (2H, d, J=8.6Hz), 7.26 (2H, d, J=8.6Hz), 6.95 (3H, s), 4.57 (2H, s), 4.13-4.00 (1H, m), 3.79 (1H, t, J=7.6Hz), 3.40-3.08 (2H, m), 2.20-1.40 (6H, m), 0.91 (3H, t, J=7.2Hz);
TLC : Rf 0.35 (acetic acid:methanol:chlorolorm=1:2:40).

Example 2(116)

4-(2R-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(2H-1,4-benzoxazin-3-on-6-yl)butanoic acid ester

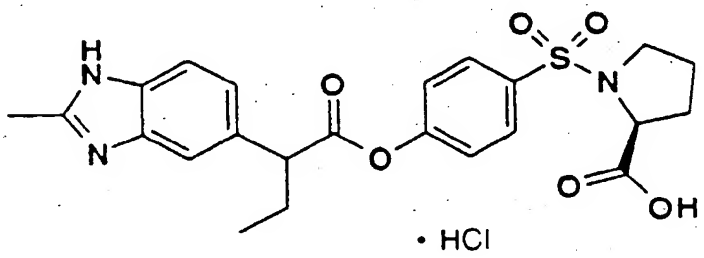


NMR (DMSO-d_6): δ 13.4-12.2 (1H, br), 10.72 (1H, s), 7.88 (2H, d, J=8.6Hz), 7.29 (2H, d, J=8.6Hz), 6.95 (3H, s),

4.57 (2H, s), 4.16-4.08 (1H, m), 3.80 (1H, t, J=7.6Hz), 3.50-3.05 (2H, m), 2.05-1.45 (6H, m), 0.91 (3H, t, J=7.2Hz);
TLC : Rf 0.36 (acetic acid:methanol:chloroform=1:2:40).

Example 2(117)

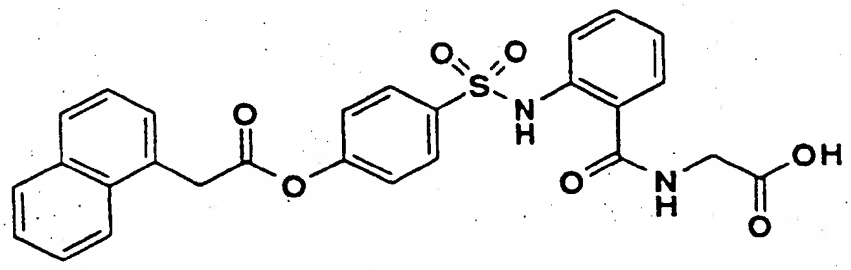
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(2-methylbenzimidazol-5-yl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 7.90-7.61 (5H, m), 7.23 (2H, d, J=9Hz), 4.23-4.17 (1H, m), 4.06 (1H, t, J=8Hz), 3.51-3.40 (1H, m), 3.31-3.20 (2H, m), 2.87 (3H, s), 2.38-2.24 (1H, m), 2.06-1.86 (3H, m), 1.76-1.64 (1H, m), 1.01 (3H, t, J=7Hz);
TLC : Rf 0.21 (chloroform:methanol:water=8:2:0.2).

Example 2(118)

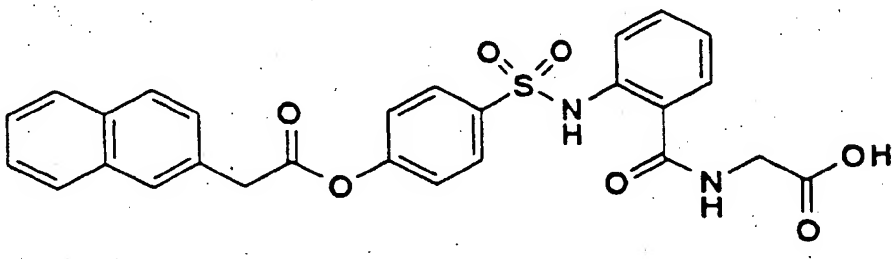
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(naphthalen-1-yl)acetic acid ester



NMR (DMSO-d_6): δ 12.74 (1H, br), 11.58 (1H, br), 9.20 (1H, t, J=5Hz), 8.08-7.70 (6H, m), 7.63-7.42 (6H, m), 7.29 (2H, d, J=9Hz), 7.17-7.10 (1H, m), 4.46 (2H, s), 3.89 (2H, d, J=6Hz);
TLC : Rf 0.28 (acetic acid:methanol:chloroform=1:2:40).

Example 2(119)

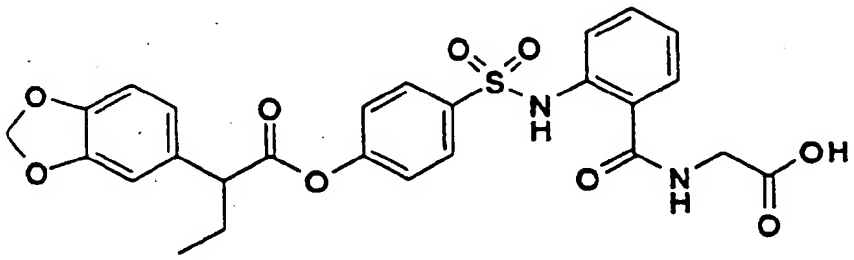
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(naphthalen-2-yl)acetic acid ester



NMR (DMSO-d_6): δ 12.67 (1H, br), 11.63 (1H, br), 9.24 (1H, t-like), 7.93-7.71 (7H, m), 7.54-7.43 (5H, m), 7.36-7.29 (2H, m), 7.18-7.10 (1H, m), 4.15 (2H, s), 3.90 (2H, d, J=6Hz);
TLC : Rf 0.31 (acetic acid:methanol:chloroform=1:2:40).

Example 2(120)

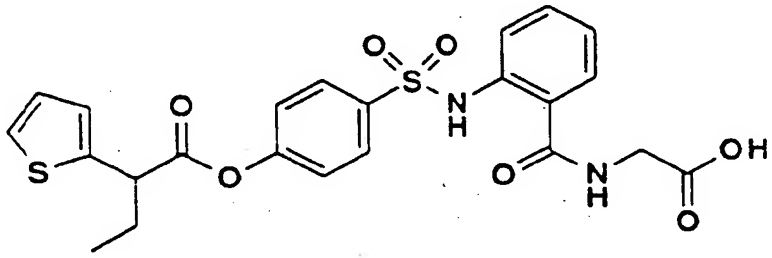
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(1,3-benzodioxol-5-yl)butanoic acid ester



NMR (DMSO-d_6): δ 12.73 (1H, br), 11.62 (1H, br), 9.22 (1H, t, J=6Hz), 7.82-7.71 (3H, m), 7.53-7.42 (2H, m), 7.26-7.10 (3H, m), 6.94-6.79 (3H, m), 6.01 (2H, s), 3.89 (2H, d, J=5Hz), 3.75 (1H, t, J=8Hz), 2.16-1.95 and 1.86-1.64 (each 1H, ml, 0.86 (3H, t, J=7Hz);
TLC : Rf 0.68 (acetic acid:methanol:chloroform=1:3:30).

Example 2(121)

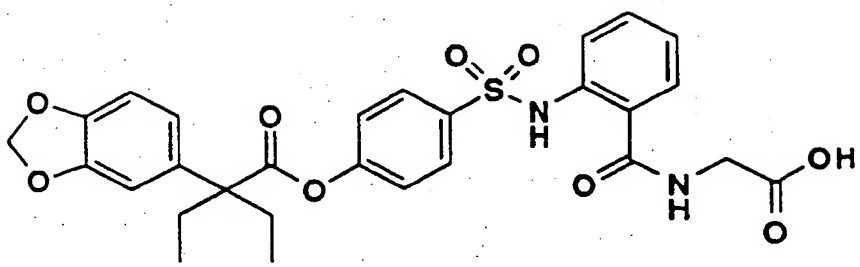
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(thiophen-2-yl)butanoic acid ester



NMR (DMSC-d_6): δ 9.4.9.2 (1H, br), 7.9-7.7 (3H, m), 7.6-7.4 (3H, m), 7.3-7.0 (5H, m), 4.19 (1H, t, J=7Hz), 3.90 (2H, d, J=5Hz), 2.2-2.0 (1H, m), 2.0-1.8 (1H, m), 0.92 (3H, t, J=7Hz);
TLC : Rf 0.18 (acetic acid:methanol:chloroform=1:2:40).

Example 2(122)

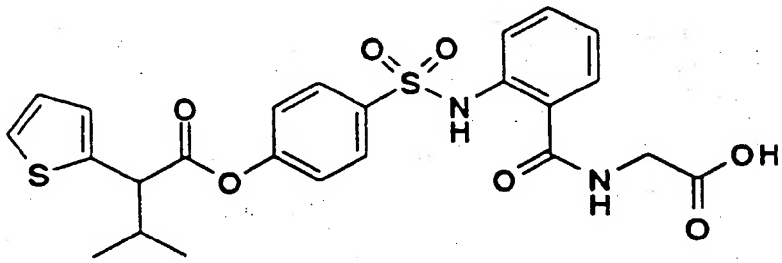
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(1,3-benzodioxol-5-yl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 12.62 (1H, br), 11.66 (1H, br), 9.24 (1H, t-like), 7.82-7.71 (3H, m), 7.52-7.42 (2H, m), 7.31-7.10 (3H, m), 6.91-6.76 (3H, m), 6.01 (2H, s), 3.89 (2H, d, J=5Hz), 2.09-1.96 (4H, m), 0.75 (6H, t, J=8Hz);
TLC : Rf 0.39 (acetic acid:methanol:chlorolorm=1:2:40).

Example 2(123)

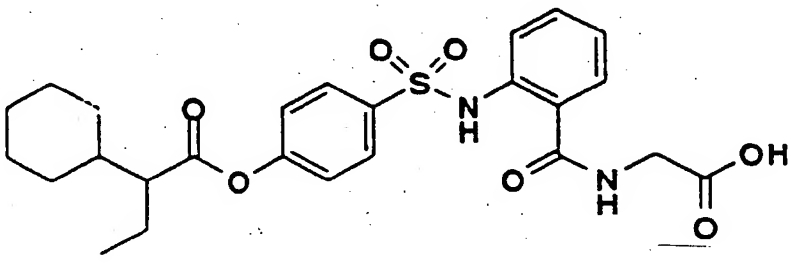
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(thiophen-2-yl)-3-methylbutanoic acid ester



NMR (DMSO-d_6): δ 12.64 (1H, br), 11.70 (1H, br), 9.24 (1H, t-like), 7.82 (2H, d, J=8Hz), 7.74 (1H, d, J=8Hz), 7.54-7.43 (3H, m), 7.26-7.00 (5H, m), 3.95 (1 H, d, J=7Hz), 3.90 (2H, d, J=6Hz), 2.36-2.18 (1H, m), 1.07 and 0.83(each 3H, each d, J=7Hz);
TLC : Rf 0.24 (acetic acid:methanol:chloroform=1:2:40).

Example 2(124)

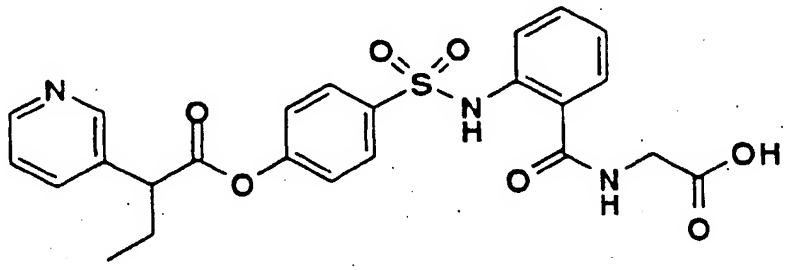
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(cyclohexane-1-yl)butanoic acid ester



NMR (DMSO-d_6): δ 12.72 (1H, br), 11.64 (1H, br), 9.27 (1H, br), 7.83 (2H, d, J=10Hz), 7.75 (1H, d, J=10Hz), 7.51 (1H, t, J=10Hz), 7.48 (1H, t, J=8Hz), 7.27 (2H, d, J=12Hz), 7.15 (1H, J=10Hz), 3.90 (2H, d, J=3Hz), 2.35-2.30 (1H, m), 1.78 (1H, d-like), 1.71-1.55 (7H, ml, 1.25-0.98 (5H, m), 0.92 (3H, t, J=7Hz);
TLC : Rf 0.30 (acetic acid:methanol:chloroform=1:2:20).

Example 2(125)

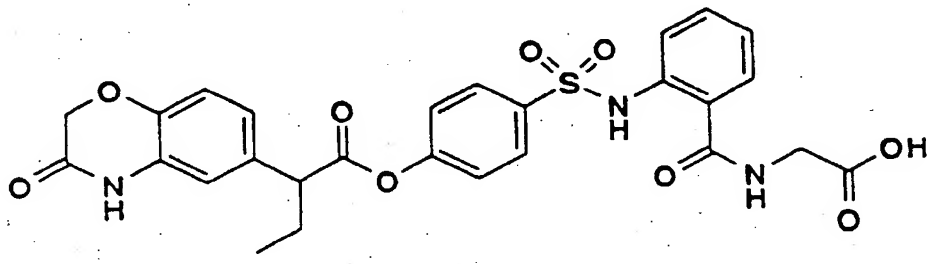
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(pyridin-3-yl)butanoic acid ester



NMR (DMSO-d_6): δ 12.00 (2H, br), 9.36 (1H, br), 8.68-8.46 (2H, br), 7.85-7.78 (4H, m), 7.50-7.10 (6H, m), 4.04-3.75 (3H, br), 2.27-2.02 and 1.96-1.74 (each 1 H, m), 0.90 (3H, br);
TLC : Rf 0.37 (acetic acid:methanol:chloroform=1:3:30).

Example 2(126)

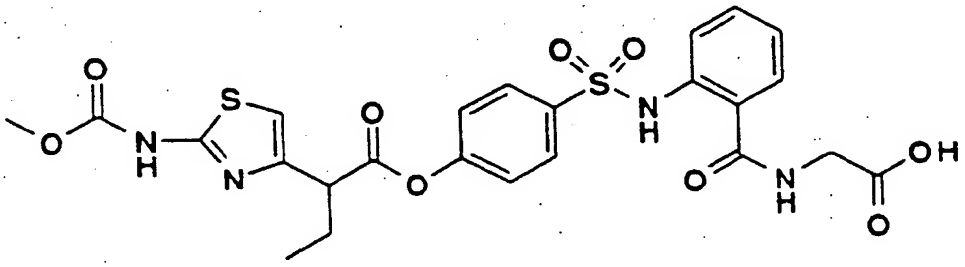
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2H-1,4-benzoxazin-3-on-6yl)butanoic acid ester



NMR (DMSO-d_6): δ 10.69 (1H, s), 9.53 (1H, t-like), 8.29 (1H, s), 7.83-7.73 (3H, m), 7.49-7.39 (2H, ml, 7.20-6.91 (6H, m), 4.55 (2H, s), 3.90-3.86 (2H, d-like), 3.73 (1H, t, J=7Hz), 2.14-1.98 and 1.80-1.66 (each 1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.38 (acetic acid:methanol:chloroform=1:3:30).

Example 2(127)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-(N-methoxycarbonylamino)thiazol-4-yl)butanoic acid ester

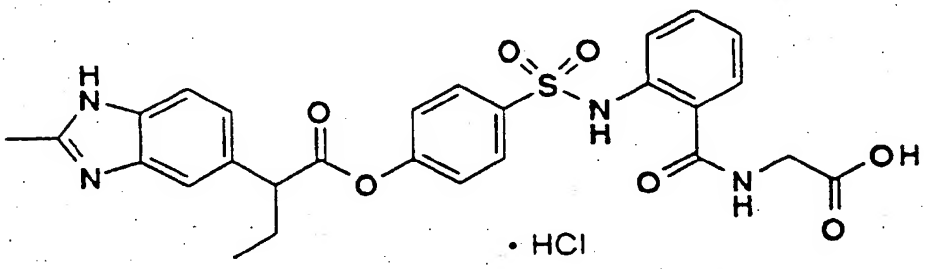


NMR (DMSO-d_6): δ 12.30 (1H, br), 11.81 (2H, br), 9.24 (1H, t-like), 7.81 (2H, d, J=7Hz), 7.74 (1H, d, J=8Hz), 7.51-7.45 (2H, m), 7.25-7.10 (3H, m), 7.07 (1H, s), 3.90 (1H, t, J=7Hz), 3.89 (2H, d, J=4Hz), 3.73 (3H, s), 2.12-1.81 (2H, m), 0.90 (3H, t, J=7Hz);

TLC : Rf 0.28 (chloroform:methanol:water=8:2:0.2).

Example 2(128)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-methylbenzimidazol-5-yl)butanoic acid ester hydrochloride

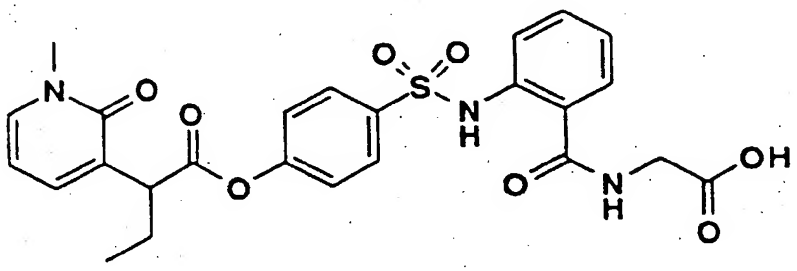


NMR (CD_3OD): δ 7.75-7.68 (4H, m), 7.63-7.57 (3H, m), 7.46-7.37 (1H, m), 7.16-7.07 (3H, m), 4.00(1H, t, J=8Hz), 3.94 (2H, s), 2.85 (3H, s), 2.34-2.15 and 2.06-1.88 (each 1H, m), 0.97 (3H, t, J=7Hz);

TLC : Rf 0.26 (chloroform:methanol:water=8:2:0.2).

Example 2(129)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(1H-1-methyl-2-pyridon-3-yl)butanoic acid ester

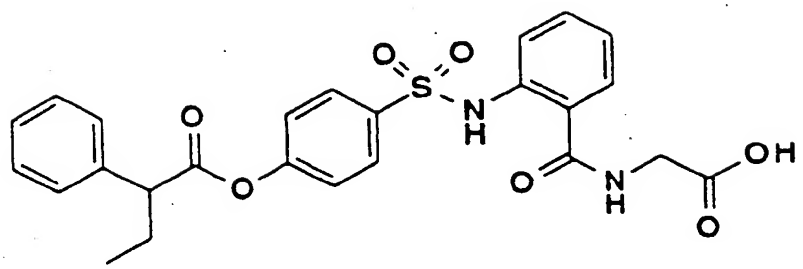


NMR (DMSO-d_6): δ 12.59 (1H, br), 11.65 (1H, br), 9.23 (1H, t-like), 7.82-7.63 (4H, m), 7.49-7.40 (3H, m), 7.25-7.09 (3H, m), 6.23 (1H, t, J=7Hz), 3.90 (2H, d, J=6Hz), 3.72 (1H, t, J=7Hz), 3.45 (3H, s), 2.04-1.70 (2H, m), 0.88 (3H, t, J=7Hz);

TLC : Rf 0.27 (chloroform:methanol:water=8:2:0.2).

Example 2(130)

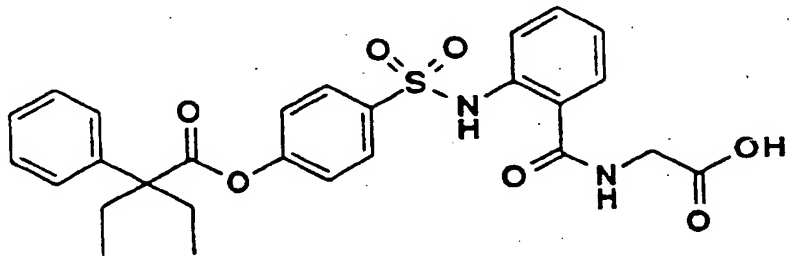
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 7.67 (3H, m), 7.50-7.20 (7H, m), 7.08 (1H, t, J=8Hz), 6.97 (2H, d, J=8Hz), 6.60 (1H, s), 5.69 (2H, brs), 4.00 (2H, m), 3.66 (1H, t, J=7Hz), 2.16 (1H, m), 1.86 (1H, m), 0.94 (3H, t, J=7Hz);
TLC : Rf 0.23 (chloroform:methanol=5:1).

Example 2(131)

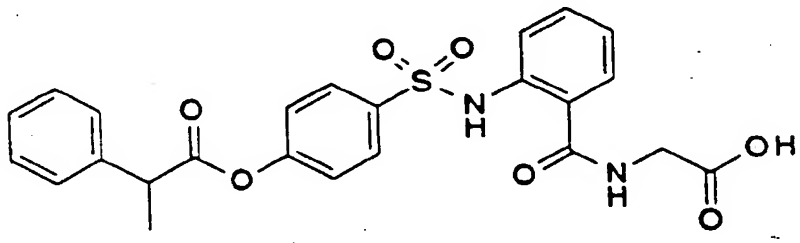
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-phenyl-2-ethylbutanoic acid ester



NMR ($DMSO-d_6$): δ 12.63 (1H, br), 11.67 (1H, br), 9.22 (1H, t-like), 7.82-7.70 (3H, m), 7.51-7.07 (10H, m), 3.89 (2H, d, J=6Hz), 2.09 (4H, m), 0.76 (6H, m);
TLC : Rf 0.58 (acetic acid:methanol;chloroform=1:3:30).

Example 2(132)

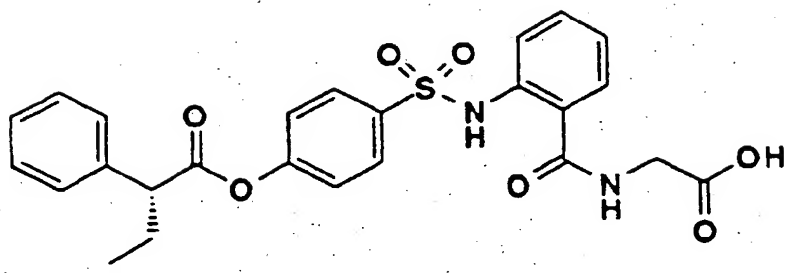
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-phenylpropanoic acid ester



NMR (d_6-DMSO): δ 12.73 (1H, br), 11.59 (1H, br), 9.25-9.19 (1H, t-like), 7.82-7.70 (3H, m), 7.50-7.10 (10H, m), 4.10 (1H, q, J=7Hz), 3.89 (2H, d, J=5Hz), 1.49 (3H, d, J=7Hz);
TLC : Rf 0.32 (acetic acid:methanol:chloroform=1:2:40).

Example 2(133)

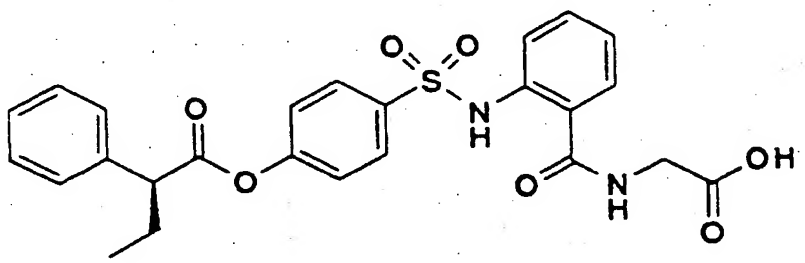
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2R-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 10.22 (1H, s), 7.71-7.65 (3H, m), 7.49-7.26 (6H, m), 7.15-7.10 (2H, m), 6.99-6.95 (2H, m), 6.49 (1H, br), 6.36 (1H, br), 4.01 (2H, d, J=5Hz), 3.65 (1H, t, J=7Hz), 2.24-2.11 and 1.95-1.81 (each 1H, m), 0.95 (3H, t, J=7Hz);
TLC : Rf 0.36 (acetic acid:methanol:chloroform=1:2:40).

Example 2(134)

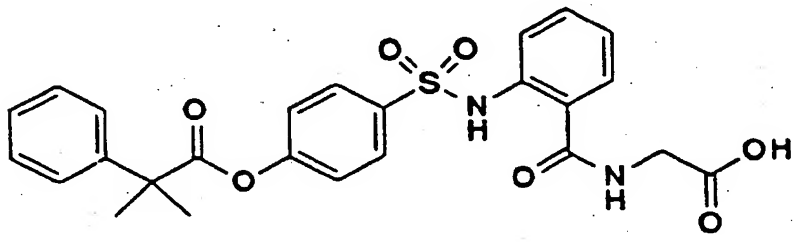
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2S-phenylbutanoic acid ester



NMR ($CDCl_3$): δ 10.29 (1H, s), 7.70-7.65 (3H, m), 7.45-7.26 (6H, m), 7.13-7.05 (2H, m), 7.00-6.96 (2H, m), 6.60 (1H, br), 4.01 (2H, d, J=5Hz), 3.66 (1H, t, J=8Hz), 2.24-2.10 and 1.95-1.81 (each 1H, m), 0.95 (3H, t, J=7Hz);
TLC : Rf 0.36 (acetic acid:methanol:chloroform=1:2:40).

Example 2(135)

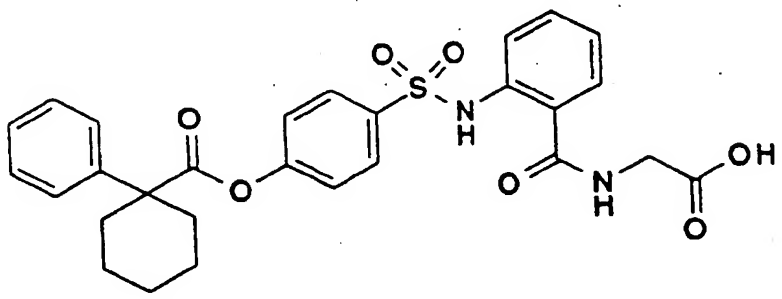
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-phenyl-2-methylpropanoic acid ester



NMR ($DMSO-d_6$): δ 12.67 (1H, br), 11.65 (1H, br), 9.22 (1H, t-like), 7.82-7.71 (3H, m), 7.52-7.09 (10H, m), 3.89 (2H, d, J=6Hz), 1.63 (6H, s);
TLC : Rf 0.34 (acetic acid:methanol:chloroform=1:3:30).

Example 2(136)

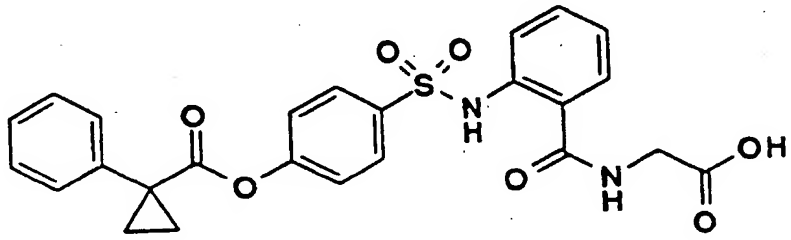
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclohexanecarboxylic acid ester



NMR (DMSO-d_6): δ 12.72 (1H, br), 11.61 (1H, br), 9.24 (1H, t-like), 7.81-7.70 (3H, m), 7.48-7.25 (7H, m), 7.14-7.10 (3H, m), 3.88 (2H, d, J=6Hz), 2.56-2.41 (2H, m), 1.85-1.23 (8H, m);
TLC : Rf 0.48 (acetic acid:methanol:chloroform=1:3:30).

Example 2(137)

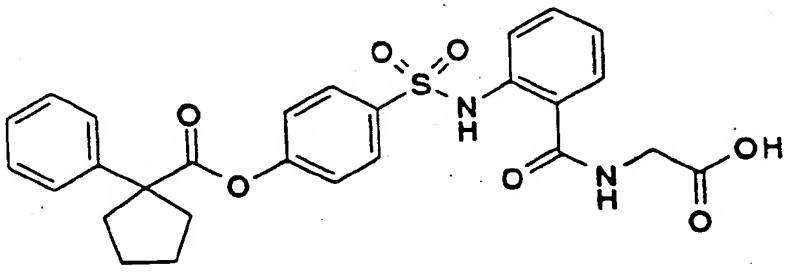
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclopropanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.3-9.1 (1H, brt), 7.8-7.6 (3H, m), 7.5.7.0 (10H, m), 3.88 (2H, d, J=5Hz), 1.68 (2H, dd, J=6,4Hz), 1.39 (2H, dd, J=6,4Hz);
TLC : Rf 0.20 (acetic acid:methanol:chloroform=1:2:40).

Example 2(138)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclopentanecarboxylic acid ester

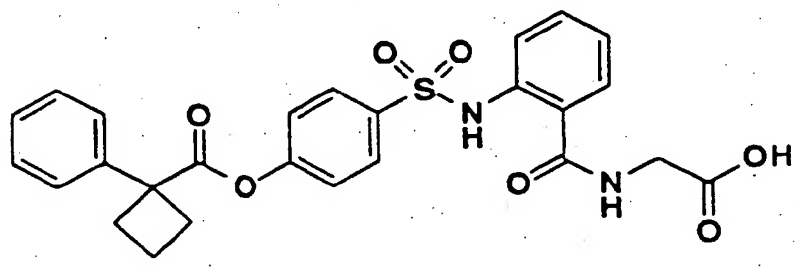


NMR (DMSO-d_6): δ 9.3-9.1 (1H, brt), 7.8-7.7 (3H, m), 7.5-7.2 (7H, m), 7.2-7.0 (3H, m), 3.87 (2H, d, J=5Hz), 2.7-2.5 (2H, m), 2.1-1.9 (2H, m), 1.9-1.6 (4H, m);

TLC : Rf 0.21 (acetic acid:methanol:chloroform=1:2:40).

Example 2(139)

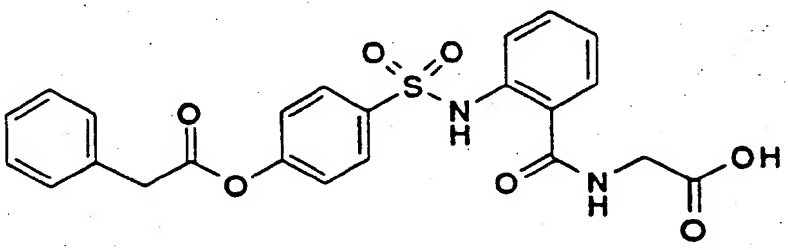
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.3-9.1 (1H, brt), 7.8-7.6 (3H, m), 7.5-7.2 (7H, m), 7.2-7.1 (3H, m), 3.88 (2H, d, J=5Hz), 3.0-2.8 (2H, m), 2.6-2.4 (2H, m), 2.1-1.8 (2H, m);
TLC : Rf 0.19 (acetic acid:methanol:chloroform=1:2:40).

Example 2(140)

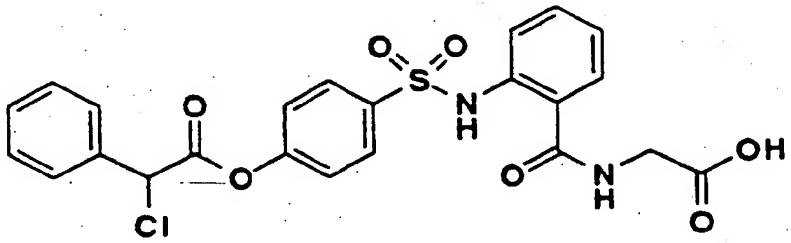
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-phenylacetic acid ester



NMR (DMSO-d_6): δ 10.01-9.76 (1H, br), 7.82-7.76 (4H, m), 7.41-7.22 (9H, m), 7.03-6.90 (1H, m), 3.96 (2H, s), 3.86 (2H, m);
TLC : Rf 0.66 (acetic acid:methanol:chloroform=1:3:30).

Example 2(141)

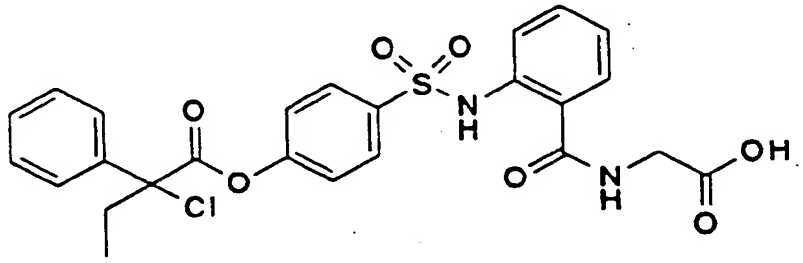
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-chloro-2-phenylacetic acid ester



NMR(DMSO-d_6): δ 9.2-9.1 (1H, brt), 7.82 (2H, d, J=8Hz), 7.71 (1H, d, J=8Hz), 7.6-7.4 (7H, m), 7.29 (2H, d, J=8Hz), 7.2.7.1 (1H, m), 6.26 (1H, s), 3.88 (2H, d, J=5Hz);
TLC : Rf 0.18 (acetic acid:methanol:chloroform=1:2:40).

Example 2(142)

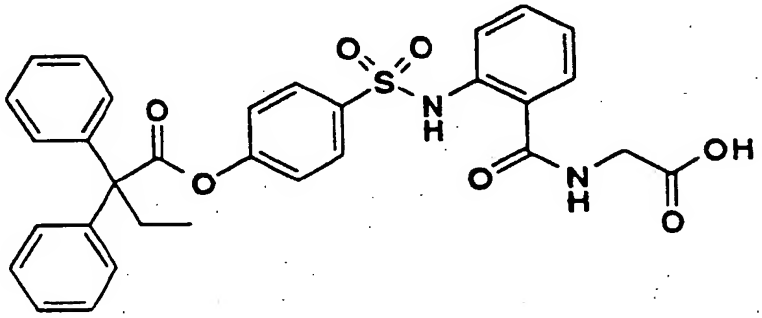
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-chloro-2-phenylbutanoic acid ester



NMR (DMSO-d_6): δ 9.3-9.2 (1H, br), 7.93 (2H, d, J=8Hz), 7.72 (1H, d, J=8Hz), 7.65-7.55 (2H, m), 7,6-7.4 (5H, m), 7.37 (2H, d, J=8Hz), 7.2-7.1 (1H, m), 3.88 (2H, d, J=5Hz), 2.6-2.4 (2H, m), 0.97 (3H, t, J=7Hz);
TLC : Rf 0.20 (acetic acid:methanol:chloroform=1:2:40).

Example 2(143)

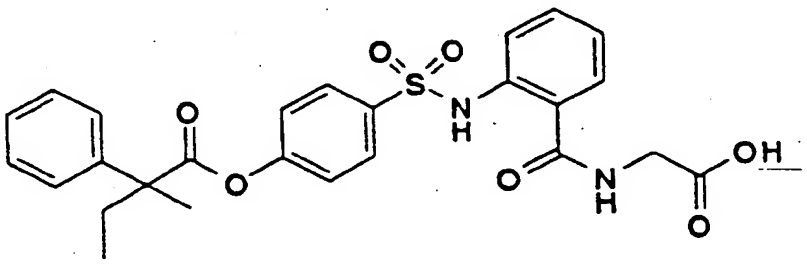
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2,2-diphenylbutanoic acid ester



NMR (DMSO-d_6): δ 9.51-9.38 (1H, m), 7.86-7.68 (4H, m), 7.51-7.20 (11 H, m), 7.19-7.01 (4H, m), 3.84 (2H, d, J=6Hz), 2.53-2.41 (2H, m), 0.79 (3H, t, J=7Hz);
TLC : Rf 0.44 (acetic acid:methanol:chloroform=1:3:30).

Example 2(144)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-methyl-2-phenylbutanoic acid ester

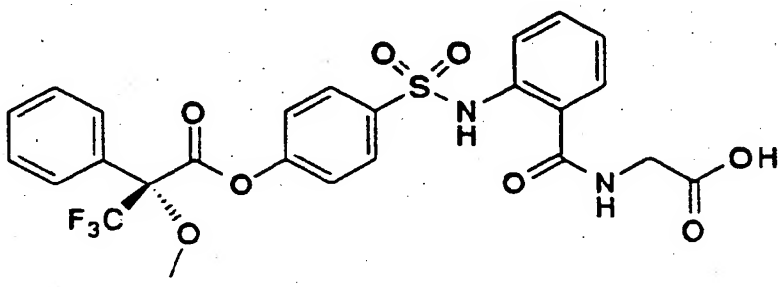


NMR (DMSO-d_6): δ 9.3-9.2 (1H, br), 7.88 (2H, d, J=8Hz), 7.70 (1H, d, J=8Hz), 7.5-7.1 (10H, m), 3.88 (2H, d,

J=5Hz), 2.2-1.9 (2H, m), 1.57 (3H, s), 0.85 (3H, t, J=7Hz);
TLC : Rf 0.15 (acetic acid:methanol:chloroform=1:2:40).

Example 2(145)

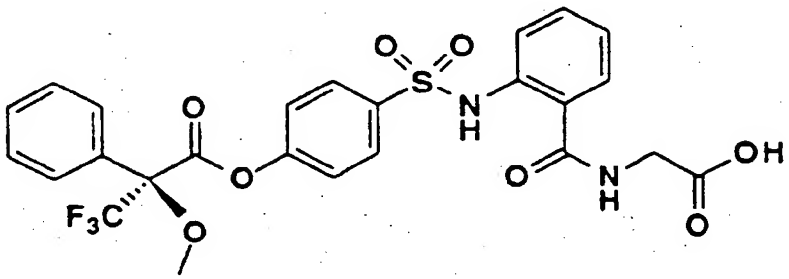
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2R-trifluoromethyl-2-phenyl-2-methoxyacetic acid ester



NMR (CD_3OD): δ 7.81 (2H, d, J=8.8Hz), 7.62 (4H, m), 7.48 (4H, m), 7.27 (2H, d, J=8.8Hz), 7.15 (1H, t, J=7.6Hz), 3.97 (2H, s), 3.65 (3H, s);
TLC : Rf 0.28 (chloroform:methanol:water=9:1:0.1).

Example 2(146)

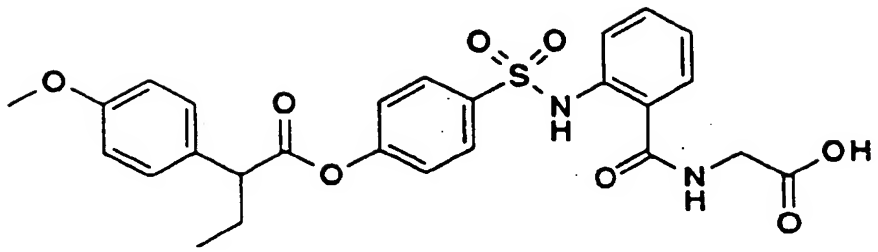
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2S-trifluoromethyl-2-phenyl-2-methoxyacetic acid ester



NMR (CD_3OD): δ 7.81 (2H, d, J=8.6Hz), 7.62 (4H, m), 7.47 (4H, m) 7.27 (2H, d, J=8.6Hz), 7.15 (1H, t, J=7.6Hz), 3.97 (2H, s), 3.65 (3H, s);
TLC : Rf 0.27 (chloroform:methanol:water=9:1:0.1).

Example 2(147)

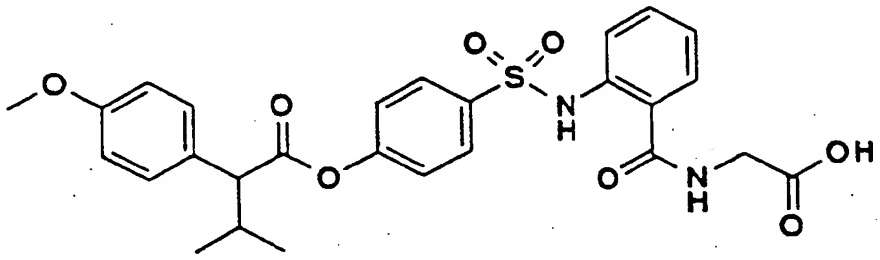
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methoxyphenyl)butanoic acid ester



NMR($CDCl_3$): δ 7.70.7.64 (2H, m), 7.42 (2H, t, J=8Hz), 7.27-7.06 (4H, m), 6.97 (2H, d, J=9Hz), 6.88 (2H, d, J=9Hz), 6.55 (1H. t-like), 4.82 (2H, brs), 3.99 (2H, d, J=5Hz), 3.79 (3H, s), 3.61 (1H, t, J=8Hz), 2.12 and 1.85(each 1H, m), 0.94 (3H, t, J=7Hz);
TLC : Rf 0.50 (acetic acid:methanol:chloroform=1:3:30).

Example 2(148)

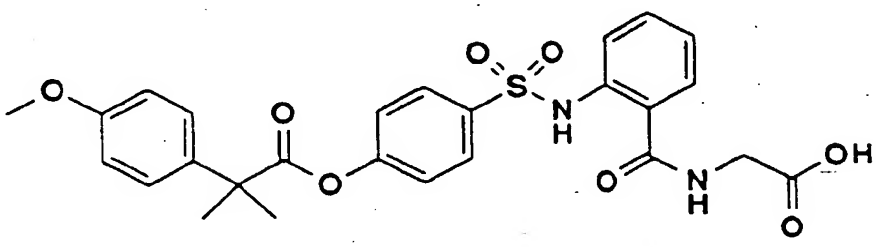
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methoxyphenyl)-3-methylbutanoic acid ester



NMR ($CDCl_3$): δ 10.20 (1H, s), 7.73-7.64 (3H, m), 7.48-7.39 (2H, m), 7.33-7.22 (2H, m), 7.12 (1H, t, J=8Hz), 6.98-6.85 (4H, m), 6.46 (1H, t-like), 5.08 (1H, br), 4.00 (2H, d, J=4Hz), 3.80 (3H, s), 3.31 (1H, d, J=10Hz), 2.46-2.27 (1H, m), 1.12 and 0.76 (each 3H, each d, J=7Hz);
TLC : Rf 0.58 (acetic acid:methanol:chloroform=1:3:30).

Example 2(149)

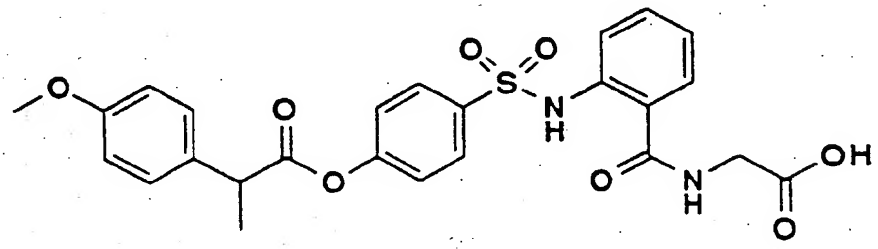
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-methylpropanoic acid ester



NMR ($DMSO-d_6$): δ 12.66 (1H, br), 11.64 (1H, br), 9.23 (1H, t-like), 7.81-7.70 (3H, m), 7.52-7.10 (7H, m), 6.92 (2H, d, J=9Hz), 3.89 (2H, d, J=6Hz), 3.74 (3H, s), 1.60 (6H, s);
TLC : Rf 0.35 (acetic acid:methanol:chloroform=1:3:30).

Example 2(150)

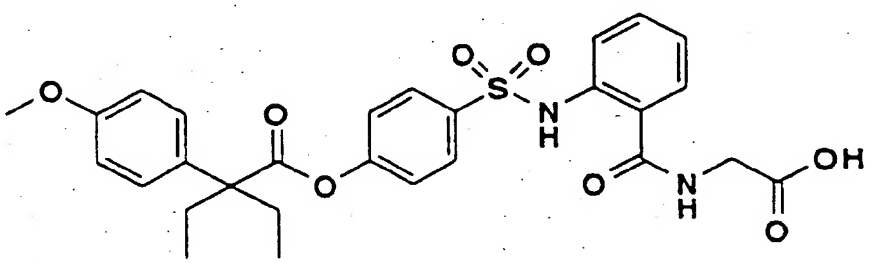
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methoxyphenyl)propanoic acid ester



NMR (DMSO-d_6): δ 12.67 (1H, br), 11.64 (1H, br), 9.21 (1H, t-like), 7.81-7.70 (3H, m), 7.52-7.41 (2H, m), 7.30-7.09 (5H, m), 6.91 (2H, d, J=8Hz), 4.00 (1H, q, J=7Hz), 3.88 (2H, d, J=5Hz), 3.73 (3H, s), 1.46 (3H, d, J=7Hz);
TLC : Rf 0.30 (acetic acid:methanol:chloroform=1:3:30).

Example 2(151)

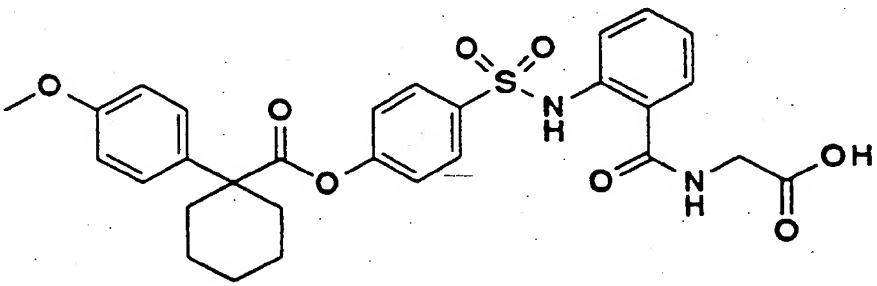
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 12.68 (1H, br), 11.62 (1H, br), 9.24 (1H, t-like), 7.82-7.71 (3H, m), 7.52-7.46 (2H, m), 7.30-7.09 (5H, m), 6.93 (2H, d, J=9Hz), 3.89 (2H, d, J=6Hz), 3.75 (3H, s), 2.10-1.98 (4H, m), 0.75 (6H, t, J=7Hz);
TLC : Rf 0.34 (acetic acid:methanol:chloroform=1:3:30).

Example 2(152)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methoxyphenyl)cyclohexanecarboxylic acid ester

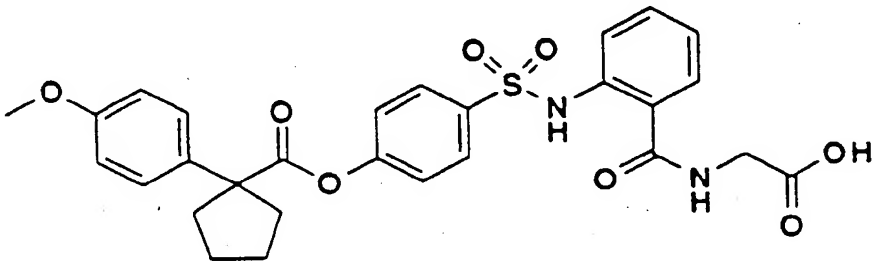


NMR (DMSO-d_6): δ 12.71 (1H, br), 11.57 (1H, br), 9.19 (1H, t-like), 7.77-7.66 (3H, m), 7.44-7.30 (4H, m), 7.13-7.04

(3H, m), 6.89 (2H, d, J=8Hz), 3.85 (2H, d, J=6Hz), 3.69 (3H, s), 2.47-2.36 (2H, m), 1.77-1.20 (8H, m);
TLC : Rf 0.51 (acetic acid:methanol:chloroform=1:3:30).

Example 2(153)

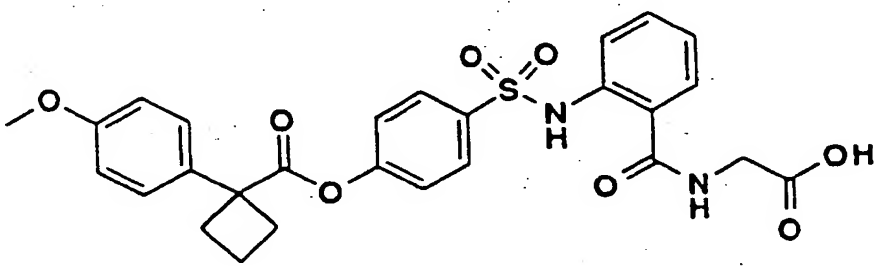
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methoxyphenyl)cyclopentanecarboxylic acid ester



NMR (DMSO-d_6): δ 12.69 (1H, br), 11.66 (1H, br), 9.23 (1H, t-like), 7.80-7.71 (3H, m), 7.51-7.29 (4H, m), 7.18-7.07 (3H, m), 6.92 (2H, dd, J=1 and 8Hz), 3.89 (2H, d, J=5Hz), 3.74 (3H, s), 2.66-2.53 (2H, m), 2.01-1.87 (2H, m), 1.79-1.67 (4H, m);
TLC : Rf 0.68 (acetic acid:methanol:chloroform=1:3:30).

Example 2(154)

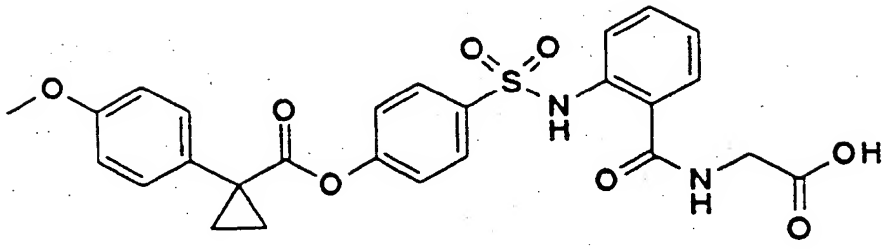
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methoxyphenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.2-9.1 (1H, brt), 7.8-7.7 (3H, m), 7.5-7.4 (2H, m), 7.30 (2H, d, J=8Hz), 7.2-7.0 (3H, m), 6.92 (2H, d, J=8Hz), 3.87 (2H, d, J=5Hz), 3.74 (3H, s), 2.9-2.7 (2H, m), 2.6-2.4 (2H, br), 2.1-1.7 (2H, br);
TLC : Rf 0.21 (acetic acid:methanol:chloroform=1:2:40).

Example 2(155)

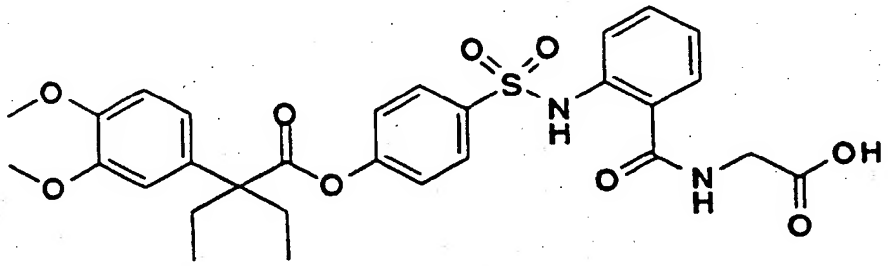
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methoxyphenyl)cyclopropanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.53-9.38 (1H, m), 7.79-7.72 (3H, m), 7.51-7.28 (4H, m), 7.26-7.19 (2H, m), 7.16-7.00 (1H, m), 6.89-6.84 (2H, m), 3.88 (2H, d, J=6Hz), 3.73 (3H, s), 1.70-1.61 (2H, m), 1.38-1.29 (2H, m);
TLC : Rf 0.49 (acetic acid:methanol:chloroform=1:3:30).

Example 2(156)

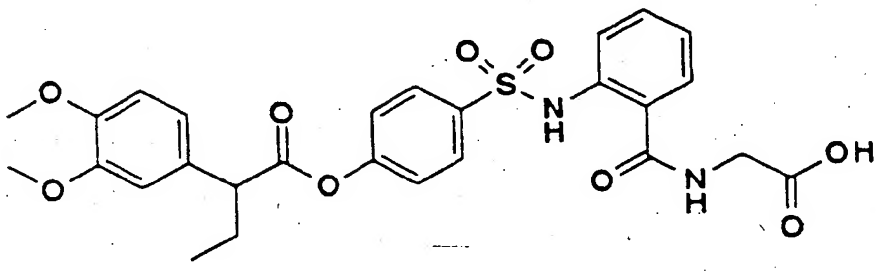
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(3,4-dimethoxyphenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 9.52-9.38 (1H, br), 7.83-7.71 (3H, m), 7.53-7.39 (2H, m), 7.19-7.02 (3H, m), 7.00-6.78 (3H, m), 3.89 (2H, d, J=6Hz), 3.76 (6H, s), 2.06 (4H, q, J=7Hz), 0.78 (6H, t, J=7Hz);
TLC : Rf 0.39 (acetic acid:methanol:chloroform=1:3:30).

Example 2(157)

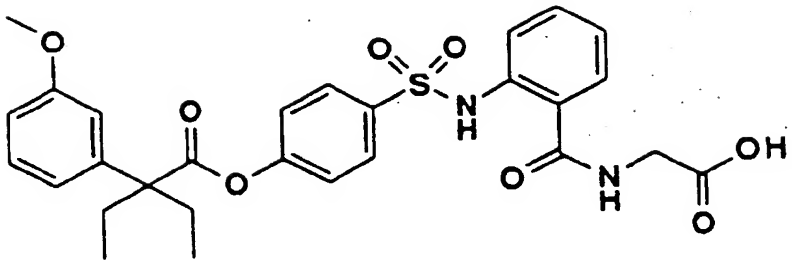
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3,4-dimethoxyphenyl)butanoic acid ester



NMR ($CDCl_3$+CD_3OD): δ 7.45-7.41 (2H, m), 7.30-7.19 (2H, m), 7.18-7.01 (1H, m), 6.82-6.69 (3H, m), 6.56-6.52 (3H, m), 3.63 (2H, s), 3.53 (6H, s), 3.28 (1H, t, J=7Hz), 1.98-1.42 (2H, m), 0.63 (3H, t, J=7Hz);
TLC : Rf 0.64 (acetic acid:methanol:chloroform=1:3:30).

Example 2(158)

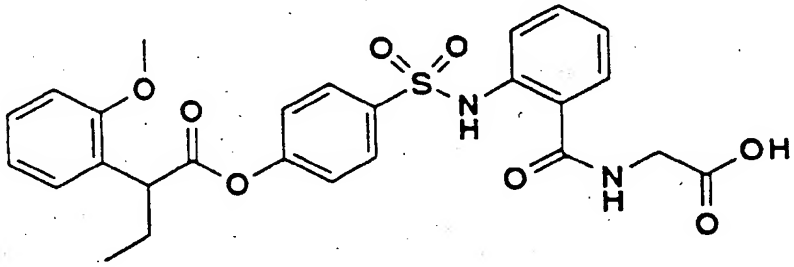
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(3-methoxyphenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 12.71 (1H, br), 11.65 (1H, br), 9.23 (1H, t-like), 7.83-7.71 (3H, m), 7.53-7.42 (2H, m), 7.35-7.10 (4H, m), 6,92-6,84 (3H, m), 3.89 (2H, d, J=6Hz), 3.75 (3H, s), 2.12-2.01 (4H, m), 0.76 (6H, t, J=7Hz);
TLC : Rf 0.39 (acetic acid:methanol:chloroform=1:2:40).

Example 2(159)

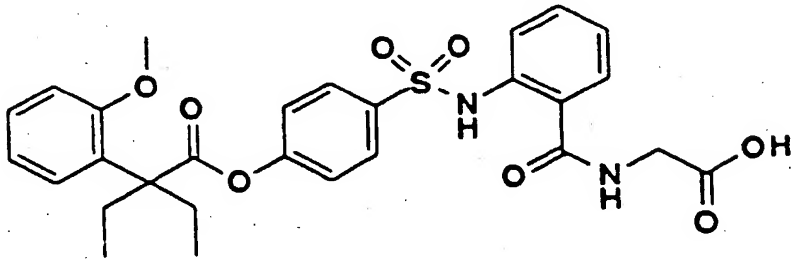
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-methoxyphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 11.58 (1H, s), 9.24-9.18 (1H, m), 7.86-7.64 (3H, m), 7.57-7.44 (2H, m), 7.38-7.09 (5H, m), 7.08-6.91 (3H, m), 4.02-3.98 (1H, m), 3.88 (2H, d, J=6Hz), 3.77 (3H, s), 2.18-1.84 (2H, m), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.41 (acetic acid:methanol:chloroform=1:3:30).

Example 2(160)

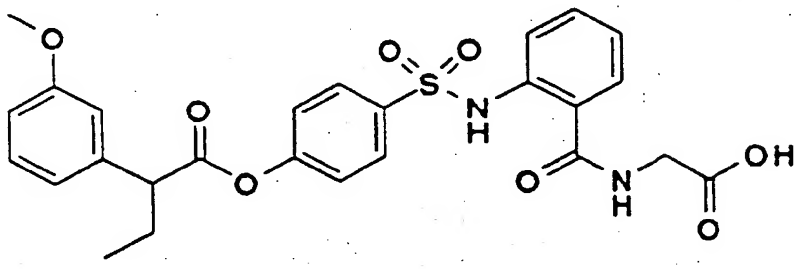
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(2-methoxyphenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 9.28-9.19 (1H, m), 7.82-7.69 (3H, m), 7.48-7.41 (2H, m), 7.28-7.08 (4H, m), 7.00-6.75 (4H, m), 3.89 (2H, d, J=6Hz), 3.77 (3H, s), 2.18-1.82 (4H, m), 0.86 (6H, t, J=7Hz);
TLC : Rf 0.39 (acetic acid:methanol:chloroform=1:3:30).

Example 2(161)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-methoxyphenyl)butanoic acid ester

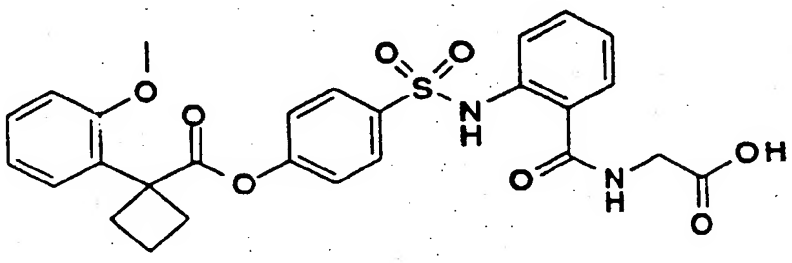


NMR (DMSO-d_6): δ 10.79 (1H, br), 7.85-7.79 (3H, m), 7.33-7.25 (2H, m), 7.17-7.06 (3H, m), 6.95-6.85 (3H, m), 6.74 (1H, t, J=7Hz), 3.85 (2H, d-like), 3.80-3.69 (1H, m), 3.75 (3H, s), 2.15-2.01 and 1.91-1.71 (each 1H, m), 0.89 (3H, t, J=7Hz).

TLC : Rf 0.47 (acetic acid:methanol:chloroform=1:2:40).

Example 2(162)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(2-methoxyphenyl)cyclobutanecarboxylic acid ester

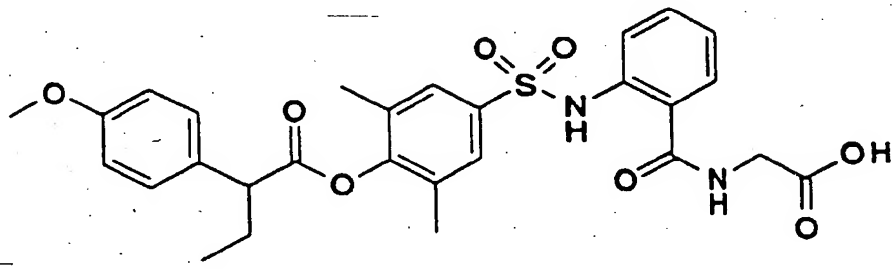


NMR (DMSO-d_6): δ 12.9-12.5 (1H, br), 11.7-11.4 (1H, br), 9.20 (1H, t-like), 7.78 (2H, d, J=8.6Hz), 7.72 (1H, d, J=7.4Hz), 7.52-7.38 (3H, m), 7.28 (1H, t-like), 7.20-7.08 (3H, m), 7.00 (2H, d, J=7.8Hz), 3.89 (2H, d, J=5.6Hz), 3.77 (3H, s), 2.85-2.65 (2H, m), 2.55-2.35 (2H, m) 2.20-2.00 and 2.00-1.80(each 1H, m);

TLC : Rf 0.30 (acetic acid:methanol:chloroform=1:2:40).

Example 2(163)

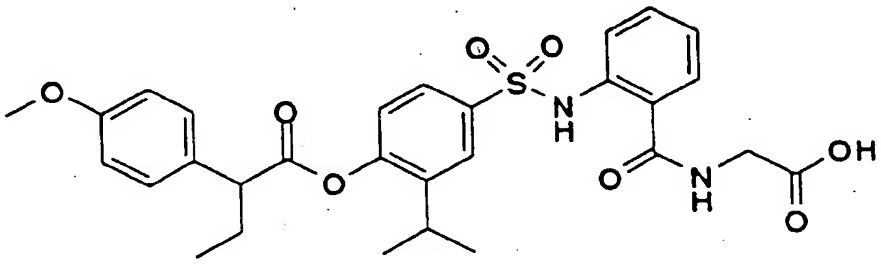
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,6-dimethylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 9.8-9.5 (brs, 1H), 7.8-7.7 (m, 1H), 7.5-7.2 (m, 6H), 7.1-6.8 (m, 4H), 4.0-3.7 (m, 3H), 3.74 (s, 3H), 2.2-1.7 (m, 8H), 0.90 (t, J=7.0Hz, 3H);
TLC : Rf 0.30 (hexane:ethyl acetate=1:1).

Example 2(164)

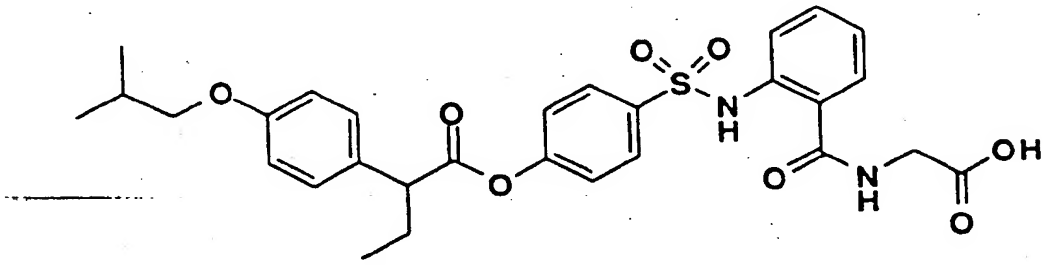
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-isopropylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester



NMR ($CDCl_3$): δ 10.0-9.9 (m, 1H), 7.8-7.7 (m, 1H), 7.6-7.2 (m, 6H), 7.2-7.0 (m, 1H), 7.0-6.8 (m, 3H), 6.5-6.3 (m, 1H), 4.0-3.4 (m, 2H), 3.80 (s, 3H), 3.64 (t, J=7.8Hz, 1H), 2.7-2.5 (m, 1H), 2.3-2.1 (m, 1H), 2.0-1.8 (m, 1H), 0.95 (t, J=7.6Hz, 3H), 0.83 (dd, J=2.0, 6.9Hz, 6H);
TLC : Rf 0.49 (chloroform:methanol=3:1).

Example 2(165)

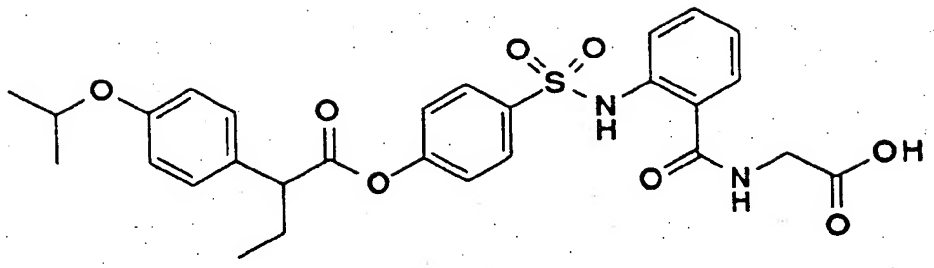
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(2-methylpropyloxy)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 9.25-9.07 (1H, br), 8.02-7.98 (1H, d-like), 7.89-7.80 (2H, d-like), 7.79-7.65 (2H, m), 7.59-7.38 (3H, m), 7.18-7.09 (1H, m), 7.01-6.77 (2H, m), 3.97- 3.65 (3H, m), 3.80 (3H, s), 3.97-3.65 (3H, s), 1.19 (6H, d, J=7Hz);
TLC : Rf 0.37 (acetic acid:methanol:chloroform=1:3:30).

Example 2(166)

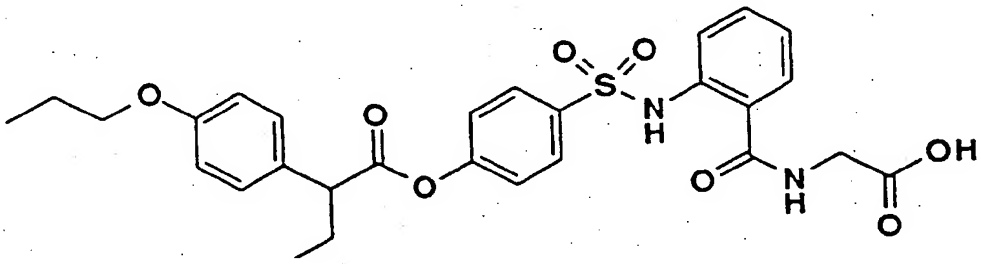
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-isopropyloxyphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 11.58 (1H, s), 9.22-9.13 (1H, m), 7.80-7.63 (4H, m), 7.49-7.40 (2H, m), 7.25-7.06 (5H, m), 6.88-6.84 (2H, m), 4.63-4.48 (1H, m), 3.88 (2H, d, J=6Hz), 3.72 (1H, t, J=7Hz), 2.18-1.63 (2H, m), 1.26 (6H, d, J=6Hz), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.34 (acetic acid:methanol:chloroform=1:3:30).

Example 2(167)

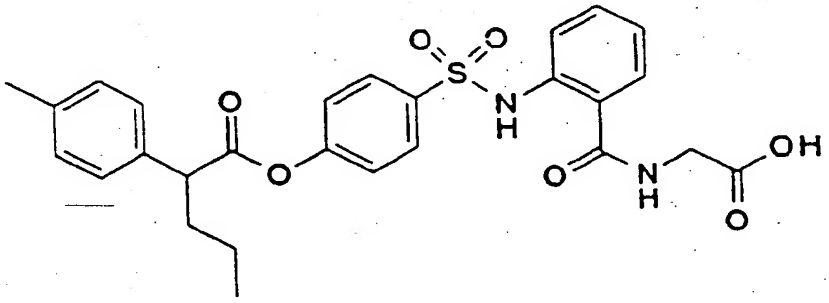
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-propyloxyphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 9.38-9.20 (1H, m), 7.81-7.77 (2H, d-like), 7.77-7.70 (2H, m), 7.49-7.31 (2H, m), 7.28-7.03 (5H, m), 6.93-6.89 (2H, d-like), 3.94-3.87 (4H, m), 3.72 (1H, t, J=6Hz), 2.20-1.98 (1H, m), 1.83-1.62 (3H, m), 0.98 (3H, t, J=7Hz), 0 88 (3H, t, J=7Hz);
TLC : Rf 0.35 (acetic acid:methanol:chloroform=1:3:30).

Example 2(168)

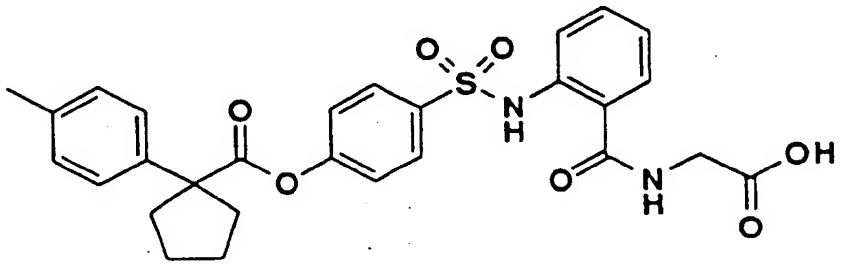
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methylphenyl)pentanoic acid ester



NMR ($CDCl_3$): δ 10.20 (1H, s), 7.68 (1H, d, J=8Hz), 7.65 (2H, d, J=8Hz), 7.50-7.35 (2H, m), 7.25-7.05 (5H, m), 6.95 (2H, d, J=8Hz), 6.6-6.5 (1H, br), 4.00 (2H, d, J=5Hz), 3.72 (1H, t, J=7Hz), 2.35 (3H, s), 2.2-2.0 (1H, m), 1.9-1.7 (1H, m), 1.4-1.2 (2H, m), 0.92 (3H, t, J=7Hz);
TLC : Rf 0.25 (chloroform:methanol:acetic acid=40:2:1).

Example 2(169)

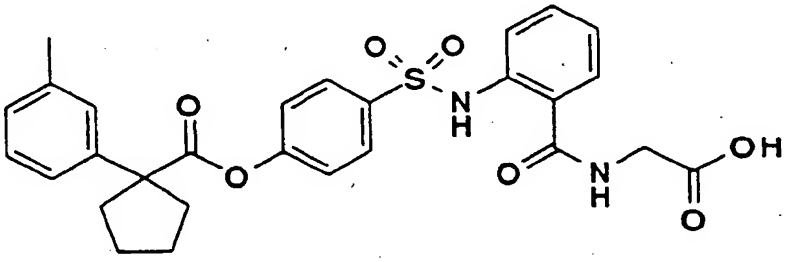
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methylphenyl)cyclopentanecarboxylic acid ester



NMR (DMSO-d_6): δ 12.70 (1H, br), 11.66 (1H, br), 9.23 (1H, t-like), 7.80-7.70 (3H, m), 7.51-7.41 (2H, m), 7.33-7.29 (2H, m), 7.19-7.09 (5H, m), 3.89 (2H, d, J=6Hz), 2.65-2.55 (2H, m), 2.29 (3H, s), 2.04-1.90 (2H, m), 1.79-1.65 (4H, m);
TLC : Rf 0.69 (acetic acid:methanol:chloroform=1:3:30).

Example 2(170)

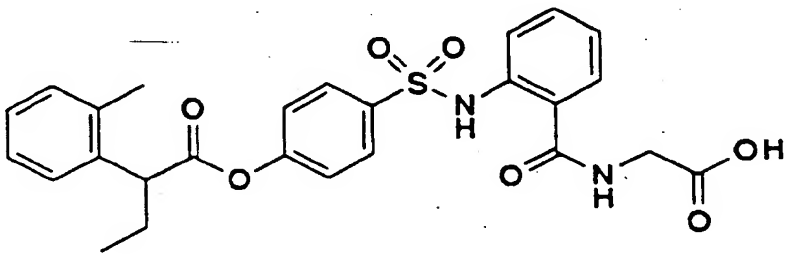
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(3-methylphenyl)cyclopentanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.22-9.18 (1H, m), 7.80-7.68 (3H, m), 7.49-7.41 (2H, m), 7.29-7.10 (7H, m), 3.89 (2H, d, J=6Hz), 2.70-2.51 (2H, m), 2.32 (3H, s), 2.04-1.83 (2H, m), 1.74-1.60 (4H, m);
TLC : Rf 0.40 (acetic acid:methanol:chloroform=1:3:30).

Example 2(171)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-methylphenyl)butanoic acid ester

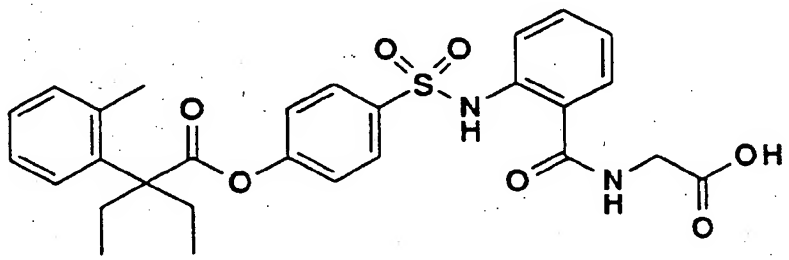


NMR (DMSO-d_6): δ 9.4-9.2 (1H, br), 7.8-7.7 (3H, m), 7.5-7.4 (2H, m), 7.3-7.0 (7H, m), 4.06 (1H, t, J=7Hz), 3.88

(2H, d, J=5Hz), 2.37 (3H, s), 2.2-2.0 (1H, m), 1.9-1.7 (1H, m), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.16 (acetic acid:methanol:chloroform=1:2:40).

Example 2(172)

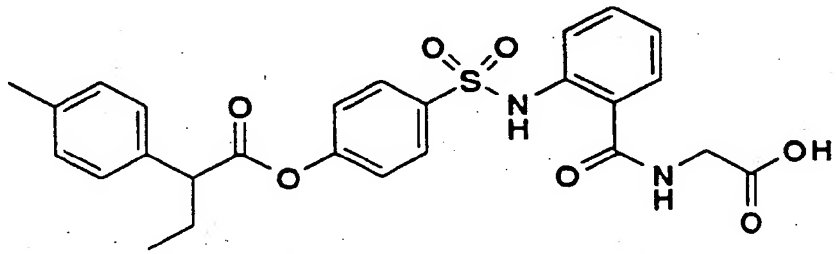
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(2-methylphenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 9.5-9.3 (1H, br), 7.9-7.6 (3H, m), 7,6-7.0 (9H, br), 4.0-3.8 (2H, br), 2.27 (3H, s), 2.3-1.9 (4H, br), 0.8-0.6 (6H, br);
TLC : Rf 0.15 (acetic acid:methanol:chloroform=1:2:40).

Example 2(173)

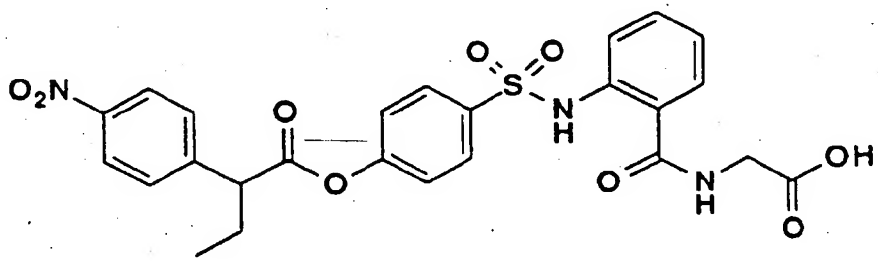
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methylphenyl)butanoic acid ester



NMR(DMSO-d_6): δ 10.61-10.32 (1H, m), 7.85-7.74 (3H, m), 7.36-7.04 (8H, m), 6.90-6.75 (1H, m), 3.92-3.83 (2H, m), 3.77 (1H, t, J=7.6Hz), 2.29 (3H, s), 2.21-1.96 and 1.89-1.63 (each 1H, m), 0.87 (3H, t, J=7.4Hz);
TLC : Rf 0.23 (chloroform:methanol:water=8:2:0.2).

Example 2(174)

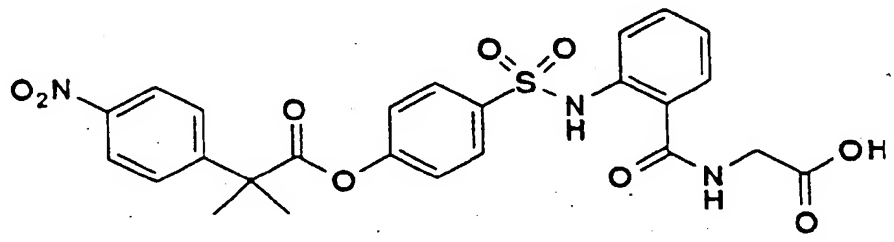
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR ($CDCl_3 + CD_3OD$): δ 8.24 (2H, d, J=8Hz), 7.85-7.55 (6H, m), 7.10 (4H, m), 3.95 (2H, s), 3.87 (1H, t, J=7Hz), 2.25 and 1.98 (each 1H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.33 (acetic acid:methanol:chloroform=1:3:30).

Example 2(175)

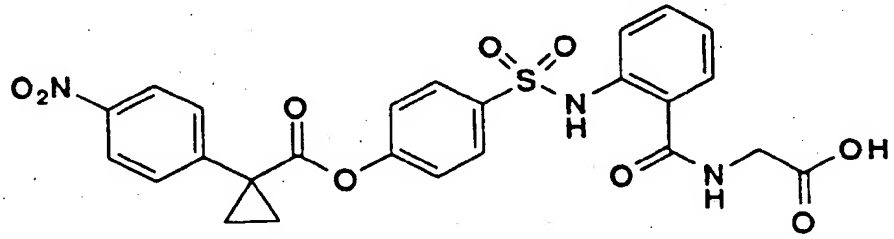
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-nitrophenyl)-2-methylpropanoic acid ester



NMR (DMSO-d_6): δ 13.50-11.00 (2H, br), 9.30-9.16 (1H, m), 8.23 (2H, d, J=8Hz), 7.88-7.68 (5H, m), 7.55-7.40 (2H, m), 7.25 (2H, d, J=8Hz),7.20-7.09 (1H, m), 3.89 (2H, d, J=6Hz), 1.68 (6H, s);
TLC : Rf 0.41 (acetic acid:methanol:chloroform=1:3:30).

Example 2(176)

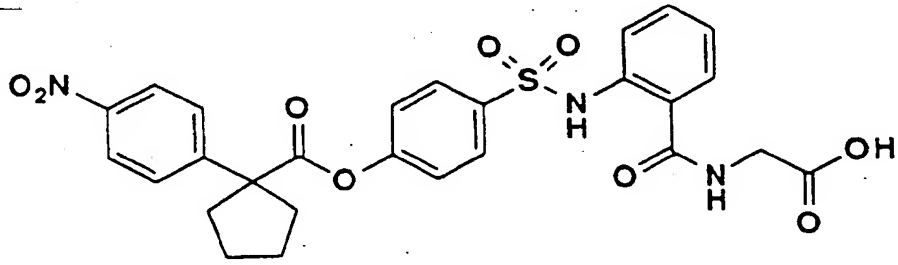
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclopropanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.2-9.1 (1H, brt), 8.18 (2H, d, J=8Hz), 7.8-7.6 (5H, m), 7.5-7.4 (2H, m), 7.29 (2H, d, J=8Hz), 7.2-7.0 (1H, m), 3.90 (2H, d, J=5Hz), 1.77 (2H, dd, J=6, 4Hz), 1.48 (2H, dd, J=6, 4Hz);
TLC : Rf 0.17 (acetic acid:methanol:chloroform=1:2:40).

Example 2(177)

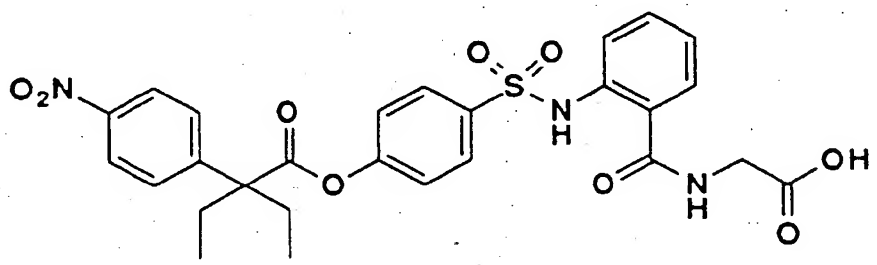
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclopentanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.2-9.1 (1H, brt), 8.22 (2H, d, J=8Hz), 7.8-7.6 (5H, m), 7.5-7.4 (2H, m), 7.2-7.1 (3H, m), 3.88 (2H, d, J=5Hz), 2.8-2.6 (2H, m), 2.2-1,9 (2H, m), 1.9-1,6 (4H, m);
TLC : Rf 0.20 (acetic acid:methanol:chloroform=1:2:40).

Example 2(178)

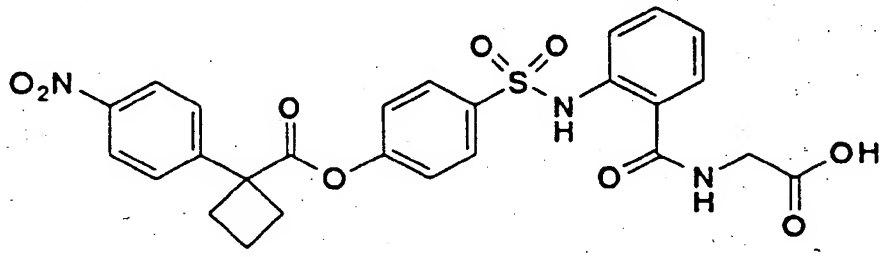
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-nitrophenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 13.40-11.20 (2H, br), 9.35-9.15 (1H, m), 8.24 (2H, d, J=8Hz), 7.82 (2H, d, J=8Hz), 7.74 (1H, t, J=8Hz), 7.67 (2H, d, J=8Hz), 7.55-7.40 (2H, m), 7.23 (2H, d, J=8Hz), 7.19-7.08 (1H, m), 3.89 (2H, d, J=6Hz), 2.25-1.98 (4H, m), 0.76 (6H, t, J=7Hz);
TLC : Rf 0.28 (acetic acid:methanol:chloroform=1:3:30).

Example 2(179)

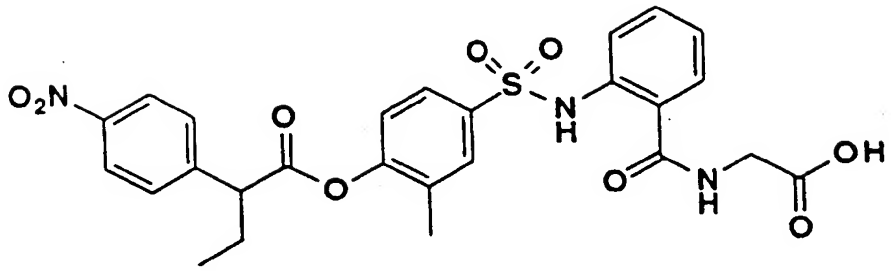
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.2-9.1 (1H, brt), 8.24 (2H, d, J=8Hz), 7.8-7.6 (5H, ml, 7.5-7,4 (2H, m), 7.3-7.1 (3H, m), 3.88 (2H, d, J=5Hz), 3.0-2.8 (2H, br), 2.7-2.5 (2H, m), 2.2-1.8 (2H, m);
TLC : Rf 0.22 (acetic acid:methanol:chloroform=1:2:40).

Example 2(180)

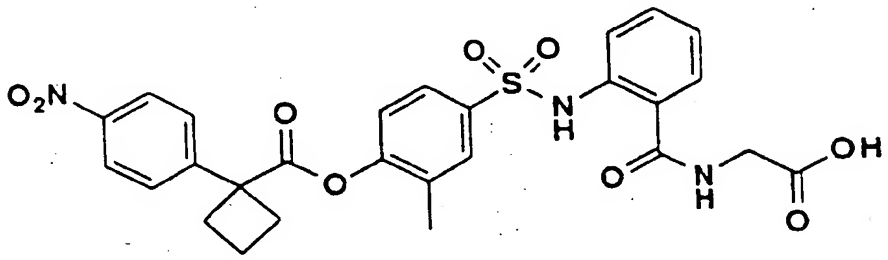
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-methylphenyl 2RS-(4-nitrophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 13.00-12.40 (1H, br), 11.80-11.40 (1H, br), 9.19 (1H, t, J=5Hz), 8.24 (2H, d, J=8Hz), 7.80-7.55 (5H, m), 7.55-7.40 (2H, m), 7.23-7.06 (2H, m), 4.15 (1H, t, J=7Hz), 3.88 (2H, d, J=5Hz), 2.19 (1H, ddq, J=14Hz, 7Hz, 7Hz), 2.05-1.75 (4H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.20 (acetic acid:methanol:chloroform=1:2:20).

Example 2(181)

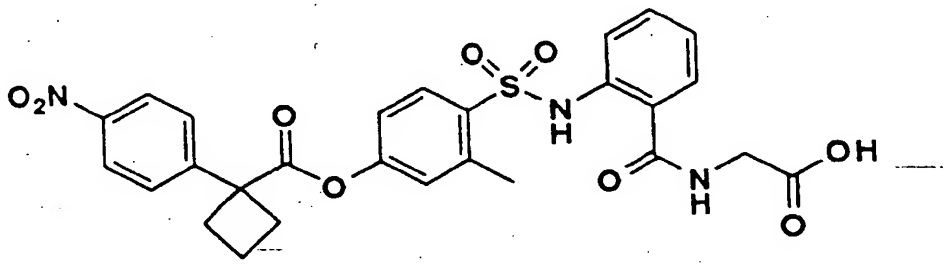
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-methylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 12.80-11.00 (2H, br), 9.20 (1 H, t, J=5Hz), 8.24 (2H, d, J=8Hz), 7.80-7.55 (5H, m), 7.55-7.37 (2H, m), 7.25-7.05 (2H, m), 3.86 (2H, d, J=5Hz), 3.04-2.85 (2H, m), 2.74-2.54 (2H, m), 2.23-1.78 (5H, m);
TLC : Rf 0.20 (acetic acid:methanol:chloroform=1:2:40).

Example 2(182)

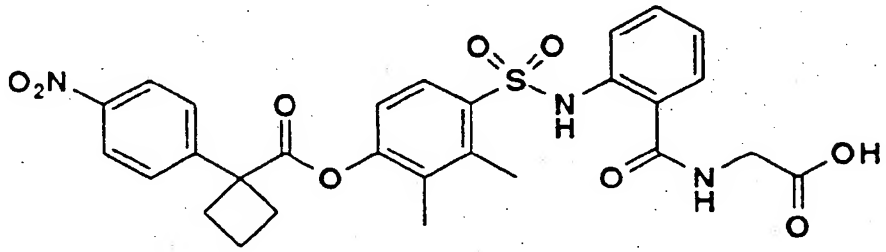
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-3-methylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 13.30-12.30 (1H, br), 12.00-11.56 (1H, br), 9.34-9.16 (1H, m), 8.26 (2H, d, J=8Hz), 7.85-7.65 (4H, m), 7.50-7.35 (2H, m), 7.22 (1H, d, J=8Hz), 7.18-7.05 (1H, m), 6.85 (1H, s), 3.97 (2H, d, J=5Hz), 3.22-3.03 (2H, m), 2.78-2.58 (2H, m), 2.28 (3H, s), 2.28-2.08 (1H, m), 2.05-1.80 (1H, m);
TLC : Rf 0.43 (acetic acid:methanol:chloroform=1:3:30).

Example 2(183)

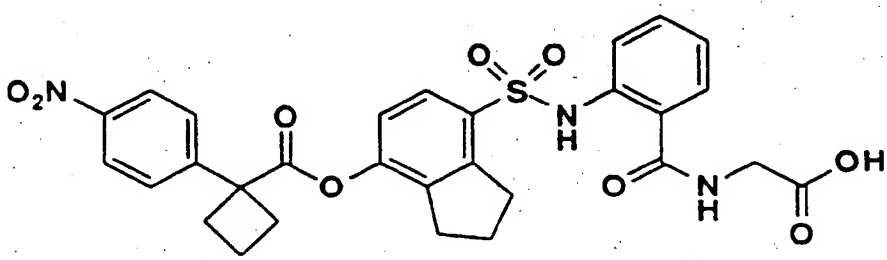
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dimethylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 13.10-12.40 (1H, br), 12.00-11.70 (1H, br), 9.35-9.22 (1H, m), 8.27 (2H, d, J=8Hz), 7.88-7.73 (3H, m), 7.65 (1H, d, J=8Hz), 7.51-7.39 (2H, m), 7.20 (1H, d, J=8Hz), 7.15-7.06 (1H, m), 4.08-3.95 (2H, m), 3.18-2.99 (1H, m), 2.99-2.78 (1H, m), 2.66-2.47 (1H, m), 2.33-2.05 (1H, m), 2.18 (3H, s), 2.05-1.82 (1H, m), 1.35 (3H, s);
TLC : Rf 0.43 (acetic acid:methanol:chloroform=1:3:30).

Example 2(184)

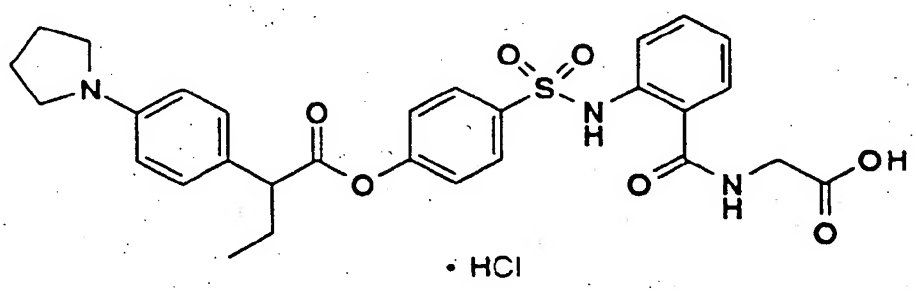
7-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dihydroinden-4-yl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 13.10-12.30 (1H, br), 12.00-11.46 (1H, br), 9.22 (1H, t, J=5Hz), 8.25 (2H, d, J=8Hz), 7.80-7.60 (4H, m), 7.50-7.34 (2H, m), 7.18-7.02 (2H, m), 3.90 (2H, d, J=5Hz), 3.14-2.78 (4H, m), 2.74-2.33 (4H, m), 2.20-1.78 (4H, m);
TLC : Rf 0.20 (acetic acid:methanol:chloroform=1:2:60).

Example 2(185)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



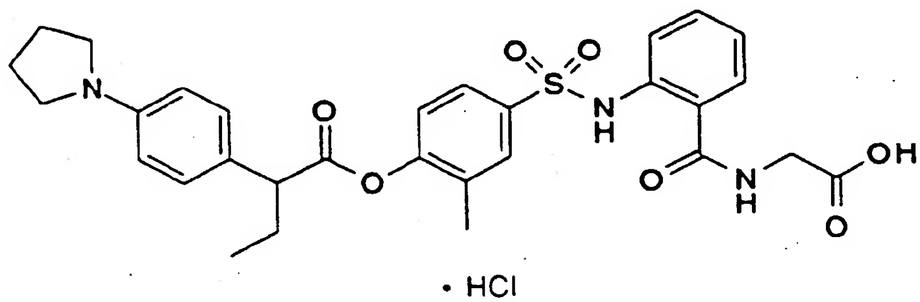
· HCl

NMR (d_6-DMSO): δ 11.60 (1H, s), 9.23 (1H, t, J=6Hz), 7.85-7.70 (3H, m), 7.55-7.40 (2H, m), 7.27-7.08 (5H, m), 6.80-6.55 (2H, m), 3.88 (2H, d, J=6Hz), 3.68 (1H, t, J=7Hz), 3.38-3.19 (4H, m), 2.20-1.86 (5H, m), 1.86-1.62 (1H, m), 0.86 (3H, t, J=7Hz);

TLC : Rf 0.44 (chloroform:methanol:acetic acid=30:2:1).

Example 2(186)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

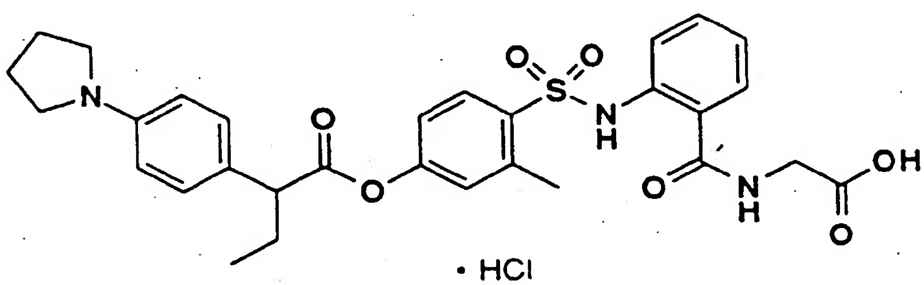


NMR (DMSO-d_6): δ 11.56 (1H, s), 9.23 (1H, t, J=5Hz), 7.83-7.55 (3H, m), 7.55-7.40 (2H, m), 7.30-7.05 (4H, m), 6.84-6.60 (2H, m), 3.88 (2H, d, J=5Hz), 3.70 (1H, t, J=7Hz), 3.40-3.13 (4H, m), 2.20-1.65 (9H, m), 0.86 (3H, t, J=7Hz);

TLC : Rf 0.45 (acetic acid:methanol:chloroform=1:3:30).

Example 2(187)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-3-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

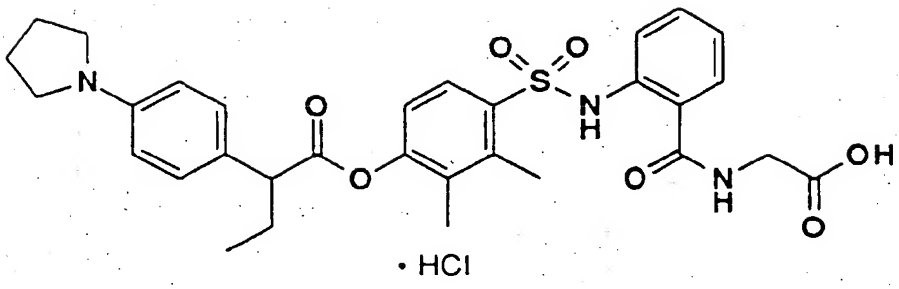


NMR (DMSO-d_6): δ 12.20 (1H, s), 9.28 (1H, t, J=5Hz), 7.85 (2H, d, J=8Hz), 7.50-7.35 (2H, m), 7.30-7.18 (3H, m), 7.18-7.03 (1H, m), 6.80 (1H, s), 6.73 (2H, d, J=8Hz), 4.00 (2H, d, J=5Hz), 3.93-3.75 (1H, m), 3.38-3.20 (4H, m), 2.28 (3H, s), 2.20-2.00 (1H, m), 2.03-1.92 (4H, m), 1.92-1.65 (1H, m), 0.88 (3H, t, J=7Hz);

TLC : Rf 0.41 (acetic acid:methanol:chloroform=1:3:30).

Example 2(188)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dimethylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

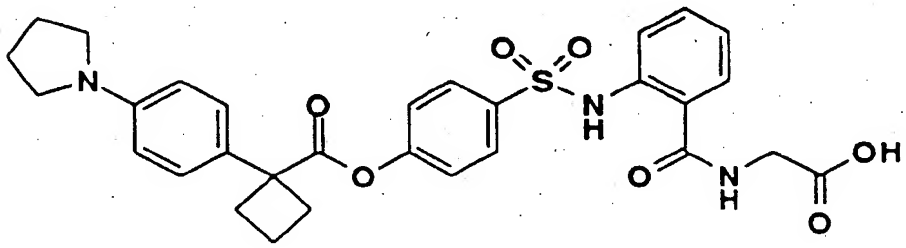


• HCl

NMR (DMSO-d_6): δ 12:09 (1H, s), 9.35-9.18 (1H, m), 7.92-7.77 (1H, m), 7.77-7.63 (1H, m), 7.46-7.38 (2H, m), 7.30-7.17 (3H. m), 7.17-7.03 (1H, m), 6.86-6.60 (2H, m), 4.02 (2H, d, J=5Hz), 3.93-3.80 (1H, m), 3.40-3.15 (4H, m), 2.19 (3H, s), 2.05-1.90 (4H, m), 1.90-1.50 (1H, m), 1.45 (3H, s), 1.30-0.98 (1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.40 (acetic acid:methanol:chloroform=1:3:30).

Example 2(189)

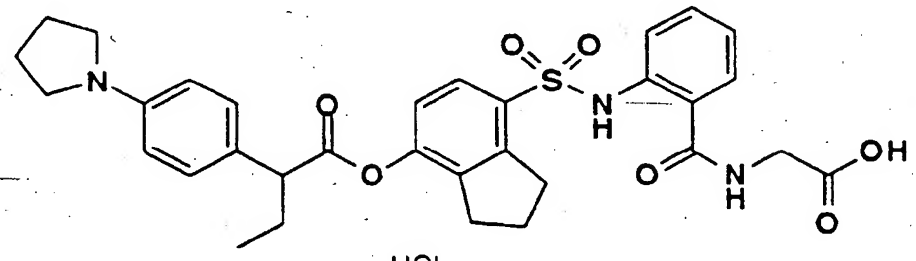
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-(pyrrolidin-1-yl)phenyl)cyclobutanecarboxylic acid ester



NMR (CD_3OD): δ 7.75-7.50 (4H, m), 7.50-7.25 (3H, m), 7.20-6.90 (5H, ml, 3.92 (2H, s), 3.46 (4H, brs), 2.90 (2H, m), 2.56 (2H, m), 2.25-1.85 (6H, m);
TLC : Rf 0.36 (acetic acid:methanol:chloroform=1:3:30).

Example 2(190)

7-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dihydroinden-4-yl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



• HCl

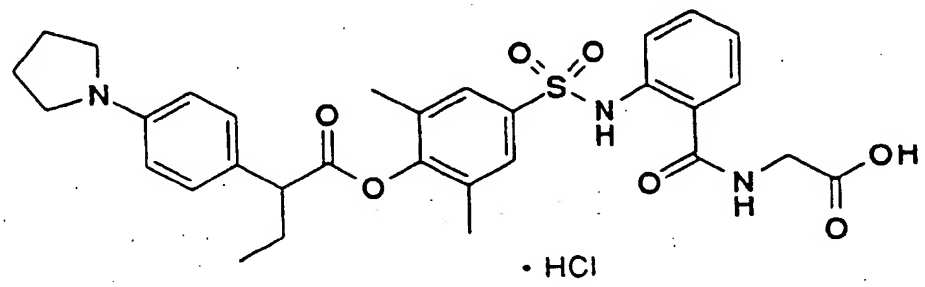
NMR (DMSO-d_6): δ 11.69 (1H, s), 9.24 (1H, t, J=5Hz), 7.75 (1H, d, J=8Hz), 7.69 (1H, d, J=8Hz), 7.50-7.38 (2H,

m), 7.19 (2H, d, J=8Hz), 7.15-7.04 (1H, m), 6.98 (1H, d, J=8Hz), 6.68 (2H, d, J=8Hz), 3.89 (2H, d, J=5Hz), 3.66 (1H, t, J=5Hz), 3.35-3.15 (4H, m), 3.15-3.00 (2H, m), 2.55-2.40 (2H, m), 2.18-1.85 (7H, m), 1,85-1.60 (1H, m), 0.86 (3H, t, J=7Hz);

TLC : Rf 0.34 (acetic acid:methanol:chloroform=1:3:30).

Example 2(191)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,6-dimethylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



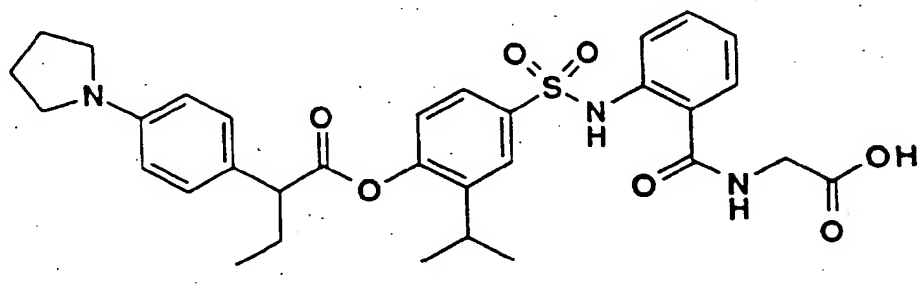
· HCl

NMR (DMSO-d_6): δ 11.49 (s, 1H), 9.3-9.2 (m, 1H), 7.8-7.1 (m, 10H), 6.8-6.6 (m, 1H), 4.0-3.7 (m, 3H), 3.4-3.1 (m, 4H), 2.2-1.7 (m, 12H), 0.89 (t, J=7.0Hz, 3H);

TLC : Rf 0.60 (chloroform:methanol=2:1).

Example 2(192)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-isopropylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



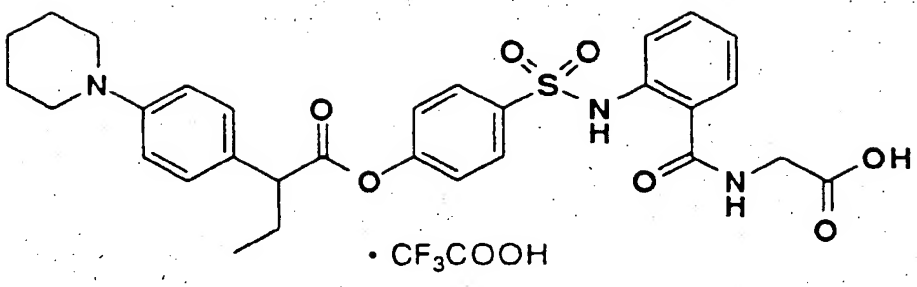
· HCl

NMR ($CDCl_3$): δ 10.04 (s, 1H), 7.8-7.7 (m, 3H), 7.6-7.5 (m, 7H), 7.2-7.1 (m, 1H), 6.9-6.8 (m, 1H), 6.4-6.3 (m, 1H), 4.0-3.6 (m, 7H), 2.8-2.7 (m, 1H), 2.4-2.2 (m, 5H), 2.0-1.8 (m, 1H), 0.98 (t, J=7.0Hz, 3H), 0.91 (d, J=7.0Hz, 6H);

TLC : Rf 0.61 (chloroform:methanol=2:1).

Example 2(193)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(piperidin-1-yl)phenyl)butanoic acid ester · trifluoroacetate

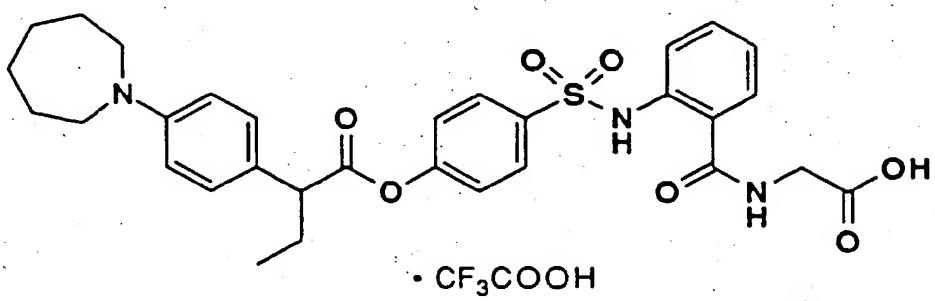


NMR (d_6-DMSO): δ 12.60-11.50 (1H, br), 9.43-9.23 (1H, br), 7.83-7.68 (3H, m), 7.52-7.35 (2H, m), 7.30-7.02 (5H, m), 6.88 (2H, d, J=8Hz), 3.88 (2H, d, J=7Hz), 3.66 (1H, t, J=8Hz), 3.20-3.05 (4H, m), 2.15-1.91 (1H, m), 1.85-1.43 (7H, m), 0.93 (3H, t, J=7Hz);

TLC : Rf 0.28 (chloroform:methanol:acetic acid=30:3:1).

Example 2(194)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(perhydroazepin-1-yl)phenyl)butanoic acid ester · trifluoroacetate

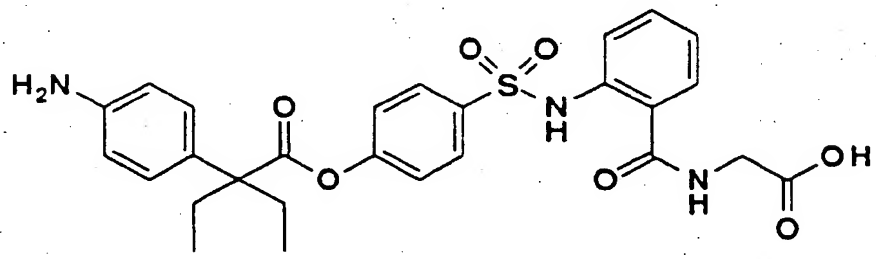


NMR (DMSO-d_6): δ 11.57 (1H, s), 9.19 (1H, t, J=7Hz), 7.85-7.65 (3H, m), 7.55-7.40 (2H, m), 7.30-7.05 (5H, m), 6.64 (2H, d, J=8Hz), 3.88 (2H, d, J=7Hz), 3.60 (1H, t, J=8Hz), 3.48-3.28 (4H, m), 2.10-1.93 (1H, m), 1.88-1.55 (5H, m), 1.55-1.30 (4H, m), 0.86 (3H, t, J=7Hz);

TLC : Rf 0.35 (acetic acid:methanol:chloroform=1:3:30).

Example 2(195)

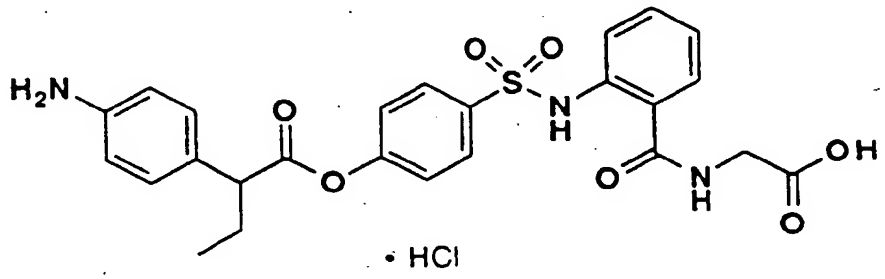
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-aminophenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 11.58 (1H, br), 9.22 (1H, t, J=5Hz), 7.80-7.70 (3H, m), 7.53-7.42 (2H, m), 7.18-7.14 (3H, m), 6.98 (2H, d, J=8Hz), 6.56 (2H, d, J=8Hz), 3.89 (2H, d, J=6Hz), 2.09-1.88 (4H, m), 0.74 (6H, t, J=7Hz);
TLC : Rf 0.40 (acetic acid:methanol:chloroform=1:3:30).

Example 2(196)

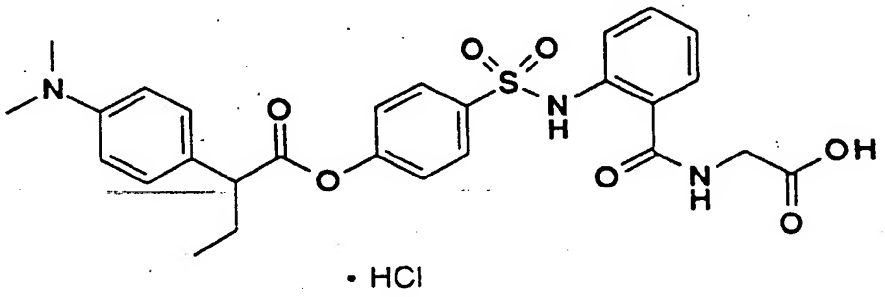
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-aminophenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 10.65 (1H, br), 7.83-7.76 (3H, m), 7.31-6.96 (6H, m), 6.80-6.73 (1H, m), 6.53 (2H, d, J=8.6Hz), 3.86 (2H, d-like), 3.55 (1H, t, J=7.4Hz), 2.12-1.90 and 1.83-1.62 (each 1H, m), 0.87 (3H, t, J=7.0Hz);
TLC : Rf 0.16 (chloroform:methanol:water=8:2:0.2).

Example 2(197)

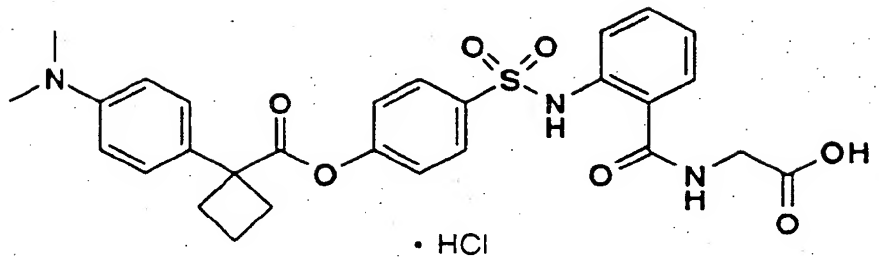
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N,N-dimethylamino)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 11.62 (1H, s), 9.25 (1H, t, J=6Hz), 7.80 (2H, d, J=9Hz), 7.76 (1H, d, J=8Hz), 7.50-7.44 (5H, m), 7.27-7.14 (4H, m), 3.89 (2H, d, J=6Hz), 3.86 (1H, t, J=8Hz), 3.04 (6H, s), 2.17-2.03 and 1.91-1.71 (each 1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.48 (acetic acid:methanol:chloroform=1:3:30).

Example 2(198)

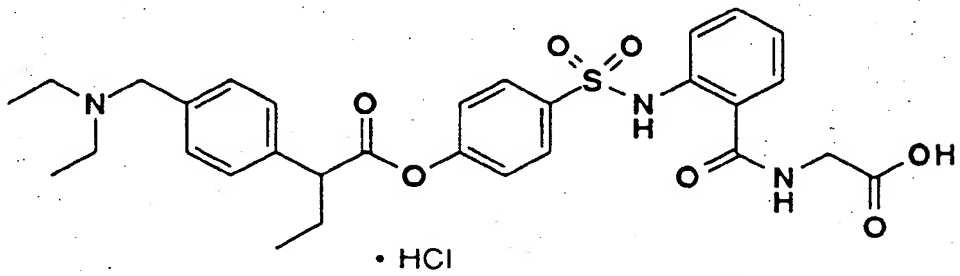
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-(N,N-dimethylamino)phenyl)cyclobutanecarboxylic acid ester · hydrochloride



NMR (DMSO-d_6): δ 11.62 (1H, s), 9.24 (1H, t-like), 7.79 (2H, d, J=8.8Hz), 7.74 (1H, d, J=8.0Hz), 7.81-7.70 (9H, m), 3.89 (2H, d, J=5.0Hz), 3.02 (6H, s), 2.93-2.80 (2H, m), 2.59-2.39 (2H, m), 2.09-1.81 (2H, m);
TLC : Rf 0.26 (chloroform:methanol:water=8:2:0.2).

Example 2(199)

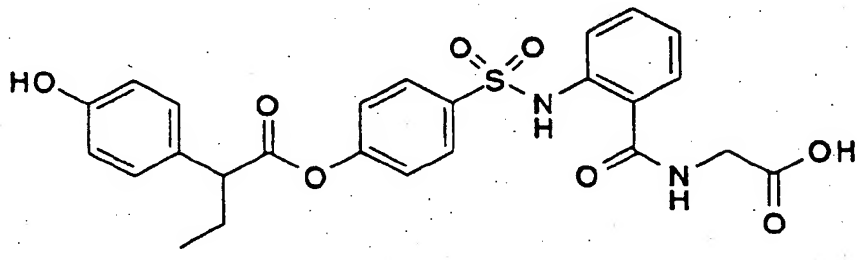
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N,N-diethylaminomethyl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 13.00-11.00 (2H, br), 9.35-9.18 (1H, m), 7.90-7.71 (3H, m), 7.68-7.56 (2H, m), 7.56-7.38 (4H, m), 7.30-7.08 (3H, m), 4.24 (2H, s), 3.99-3.79 (2H, m), 3.71-3.65 (1H, m), 3.10-2.90 (4H, m), 2.11 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.82 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.23 (6H, t, J=7Hz), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.18 (acetic acid:methanol:chloroform=1:2:20).

Example 2(200)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-hydroxyphenyl)butanoic acid ester

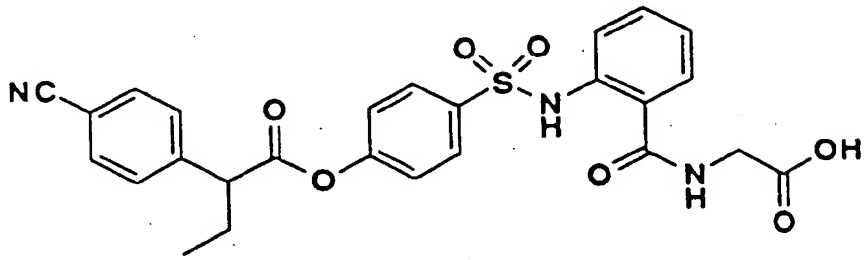


NMR (DMSO-d_6): δ 12.90-11.20 (2H, br), 9.39 (1H, br), 9.22 (1H, t-like), 7.79 (2H, d, J=8.8Hz), 7.73 (1H, d, J=7.8Hz), 7.53-7.42 (2H, m), 7.19-7.12 (5H, m), 6.74 (2H, d, J=8.6Hz), 3.89 (2H, d, J=5.6Hz), 3.68 (1H, t, J=7.6Hz), 2.11-1.93 and 1.84-1.62 (each 1H, m), 0.86 (3H, t, J=7.2Hz);

TLC : Rf 0.12 (chloroform:methanol:water=8:2:0.2).

Example 2(201)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-cyanophenyl)butanoic acid ester

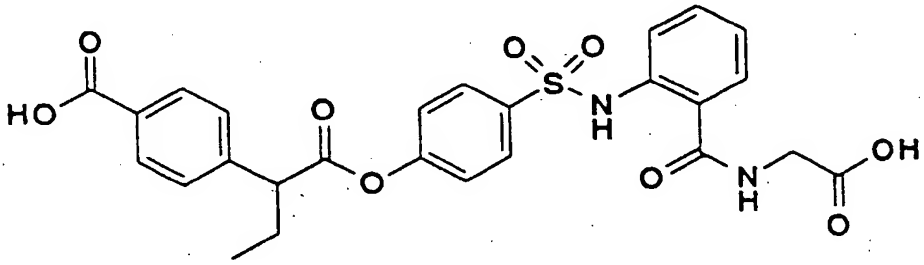


NMR (DMSO-d_6): δ 10.72-10.41 (1H, m), 7.88-7.69 (5H, m), 7.59 (2H, d, J=8.2Hz), 7.29 (2H, d, J=8.2Hz), 7.22-7.06 (3H, m), 6.78 (1H, t, J=8.2Hz), 4.01 (1H, t, J=7.4Hz), 3.91-3.77 (2H, m), 2.24-2.01 and 1.95-1.70 (each 1H, m), 0.88 (3H, t, J=7.4Hz);

TLC : Rf 0.24 (chloroform:methanol:water=8:2:0.2).

Example 2(202)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-carboxyphenyl)butanoic acid ester

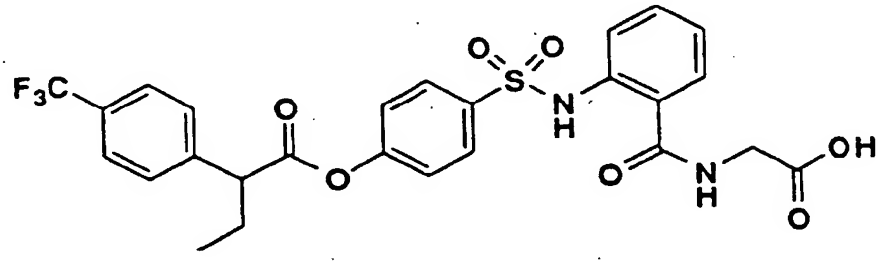


NMR (DMSO-d_6): δ 11.36 (1H, s), 10.45 (1H, s), 9.16 (1H, t-like), 7.90 (2H, d, J=8Hz), 7.71 (1H, d, J=8Hz), 7.60-7.38 (7H, m), 7.18-7.03 (1H, m), 6.81 (2H, d, J=8Hz), 3.89 (2H, d, J=6Hz), 3.40 (1H, t, J=7Hz), 2.04-1.58 (2H, m), 0.83 (3H, t, J=7Hz);

TLC : Rf 0.53 (acetic acid:methanol:chloroform=1:5:15).

Example 2(203)

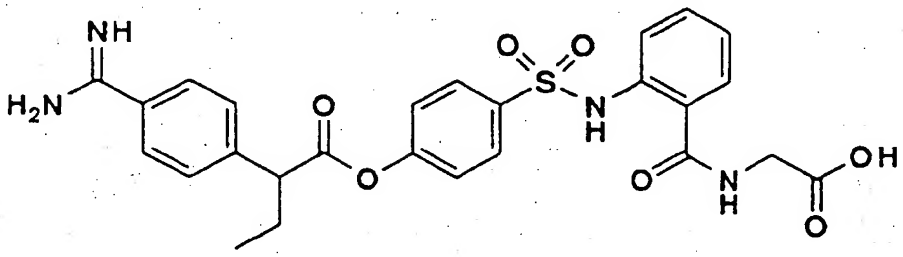
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-trifluoromethylphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 10.75-10.45 (1H, m), 7.87-7.56 (7H, m), 7.35-7.07 (4H, m), 6.87-6.72 (1H, m), 4.02 (1H, t, J=7.7Hz), 3.93-3.82 (2H, m), 2.25-2.02 and 1.95-1.71 (each 1H, m), 0.89 (3H, t, J=7.0Hz);
TLC : Rf 0.23 (chloroform:methanol:water=8:2:0.2).

Example 2(204)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-amidinophenyl)butanoic acid ester · trifluoroacetate

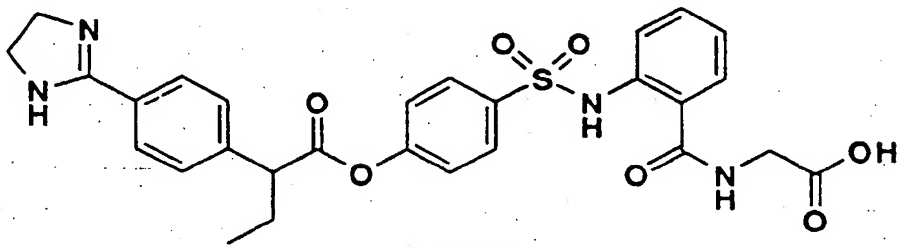


· CF_3COOH

NMR (DMSO-d_6): δ 10.42-10.20 (1H, m), 9.95-9.44 (2H, m), 9.44-8.90 (2H, m), 7.86-7.66 (4H, m), 7.66-7.30 (4H, m), 7.30-7.04 (3H, m), 6.88-6.75 (1H, m), 4.01 (1H, t, J=7Hz), 3.90-3.79 (2H, m), 2.26-2.03 (1H, m), 1.95-1.74 (1H, m), 0.96-0.76 (3H, m);
TLC : Rf 0.40 (acetic acid:methanol:chloroform=1:2:10).

Example 2(205)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(imidazolin-2-yl)phenyl)butanoic acid ester · trifluoroacetate

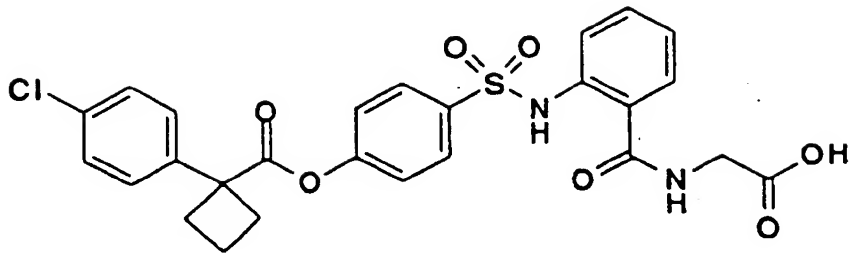


· CF_3COOH

NMR (DMSO-d_6): δ 10.60-10.34 (1H, m), 7.95 (2H, d, J=8Hz), 7.82-7.71 (3H, m), 7.64 (2H, d, J=8Hz), 7.34 (1H, d, J=8Hz), 7.26-7.00 (4H, m), 6.80 (1H, t, J=8Hz), 4.60-3.93 (7H, m), 2.15 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.94-1.71 (1H, m), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.2 (acetic acid:methanol:chloroform=1:2:10).

Example 2(206)

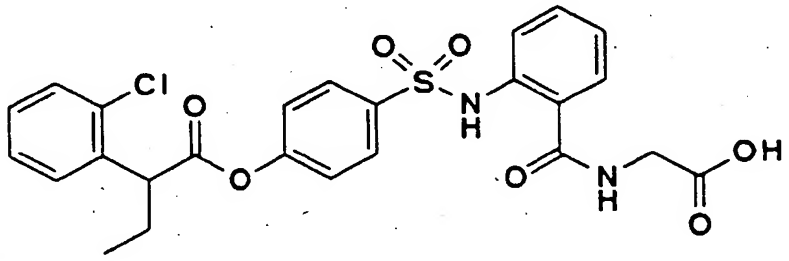
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-chlorophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 9.3-9.1 (1H, brt), 7.8-7.6 (3H, m), 7.5-7.3 (6H, m), 7.2-7.0 (3H, m), 3.88 (2H, d, J=5Hz), 3.0-2.8 (2H, m), 2.6-2.4 (2H, m), 2.2-1.8 (2H, m);
TLC : Rf 0.22 (acetic acid:methanol:chloroform=1:2:40).

Example 2(207)

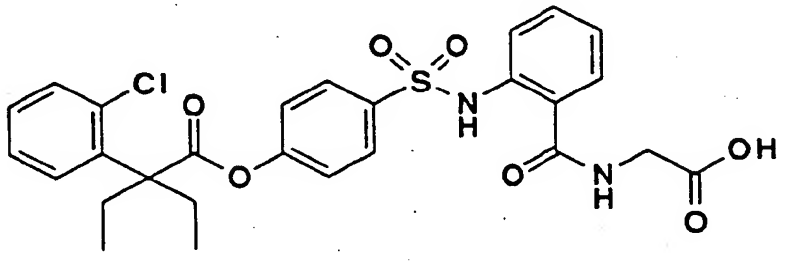
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-chlorophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 9.4-9.2 (1H, br), 7.8-7.7 (3H, m), 7.5-7.3 (6H, m), 7.3-7.0 (3H, m), 4.24 (1H, t, J=7Hz), 3.88 (2H, d, J=5Hz), 2.2-2.0 (1H, m), 2.0-1.8 (1H, m), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.16 (acetic acid:methanol:chloroform=1:2:40).

Example 2(208)

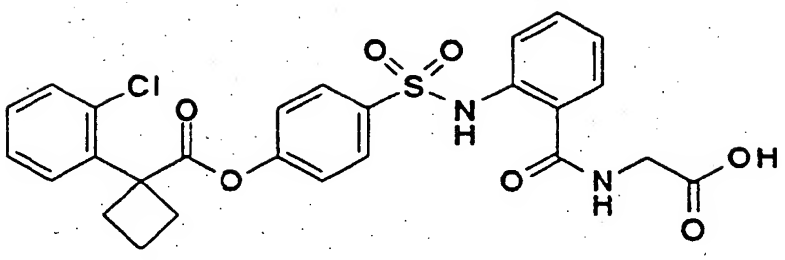
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(2-chlorophenyl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 9.5-9.3 (1H, br), 7.82 (2H, d, J=8Hz), 7.72 (1H, d, J=8Hz),7.6-7.3 (6H, m), 7.23 (2H, d, J=8Hz), 7.09 (1H, t, J=8Hz), 3.90 (2H, d, J=5Hz), 2.4-2.1 (2H, m), 2.2-1.9 (2H, m), 0.70 (6H, t, J=7Hz);
TLC : Rf 0.12 (acetic acid:methanol:chloroform=1:2:40).

Example 2(209)

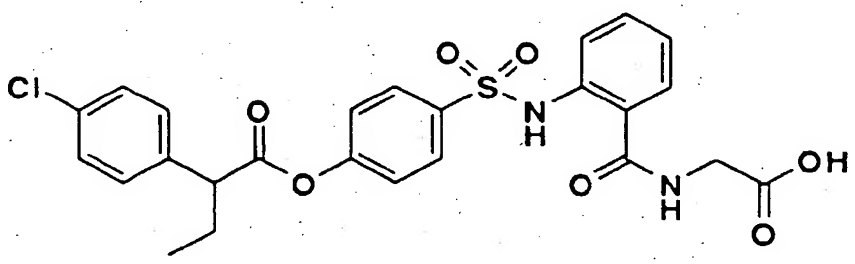
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(2-chlorophenyl)cyclobutanecarboxylic acid ester



NMR ($CDCl_3$+CD_3OD): δ 7.72 (2H, d, J=8.5Hz), 7.68-7.05 (8H, m), 7.02 (2H, d, J=8.5Hz), 3.99 (2H, s), 3.01-2.82 (2H, m), 2.75-2.50 (2H, m), 2.41-2.15 (1H, m), 2.10-1.80 (1H, m);
TLC : Rf 0.30 (acetic acid:methanol:chloroform=1:2:40).

Example 2(210)

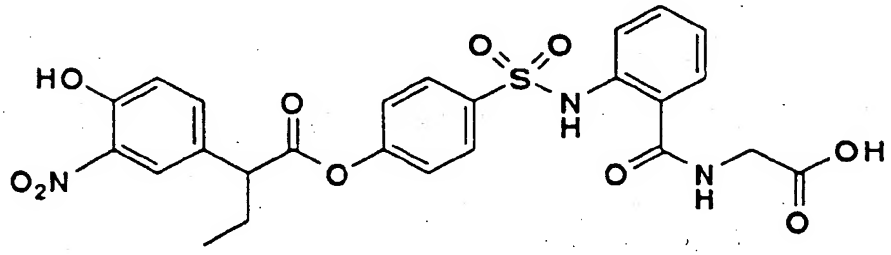
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-chlorophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 10.47-10.18 (1H, m), 7.86-7.74 (3H, m), 7.51-7.08 (8H, m), 6.93-6.81 (1H, m), 3.95-3.82 (3H, m), 2.20-1.96 and 1.90-1.66 (each 1H, m), 0.87 (3H, t, J=7.4Hz);
TLC : Rf 0.26 (chloroform:methanol:water=8:2:0.2).

Example 2(211)

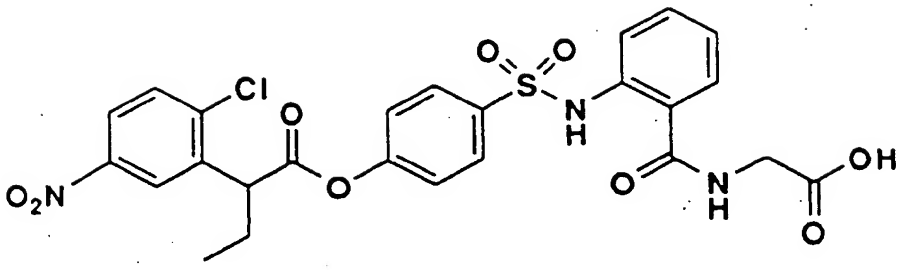
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-hydroxyphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 9.36 (1H, t-like), 7.90-7.72 (4H, m), 7.58-7.40 (3H, m), 7.24-7.07 (4H, m), 3.90 (2H, d, J=6Hz), 2.20-1.97 and 1.89-1.69 (each 1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.21 (acetic acid:methanol:chloroform=1:2:40).

Example 2(212)

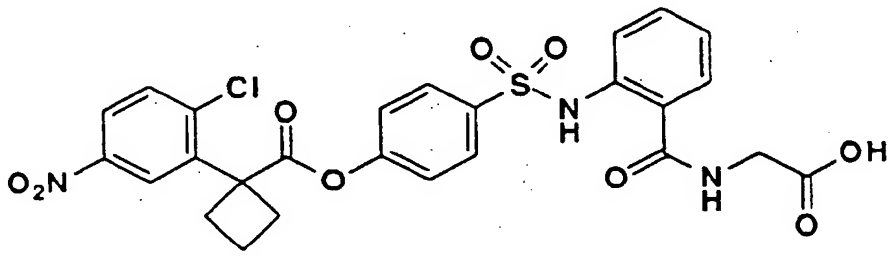
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-chloro-5-nitrophenyl)butanoic acid ester



NMR(DMSO-d_6): δ 12.10 (2H, br), 9.26 (1H, t-like), 8.32 (1H, t, J=3Hz), 8.20 (1H, dd, J=3 and 9Hz), 7.85-7.79 (3H, m), 7.73 (1H, d, J=8Hz), 7.52-7.41 (2H, m), 7.27 (2H, d, J=9Hz), 7.15-7.08 (1H, m), 4.43 (1H, t, J=6Hz), 3.89 (2H, d, J=6Hz), 2.32-2.18 and 2.09-1.91 (each 1H, m), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.51 (acetic acid:methanol:chloroform=1:3:30).

Example 2(213)

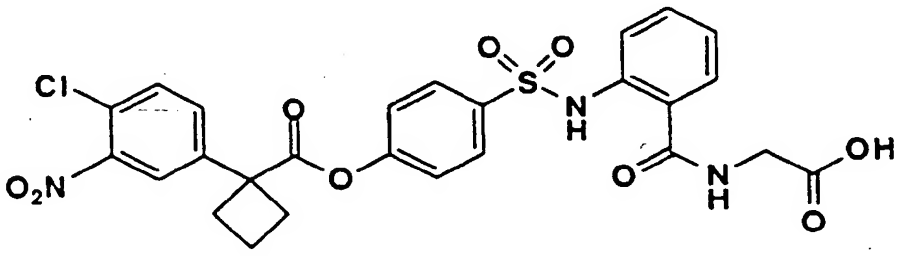
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(2-chloro-5-nitrophenyl)cyclobutanecarboxylic acid ester



NMR ($CDCl_3$+CD_3OD): δ 8.32 (1H, d, J=2.5Hz), 8.14 (1H, dd, J=2.5, 8.5Hz), 7.76 (2H, d, J=8.5Hz), 7.62 (2H, t, J=8.5Hz), 7.53 (1H, d, J=8.5Hz), 7.43 (1H, d, J=8.5Hz), 7.12 (1H, d, J=8.5Hz), 7.06 (2H, d, J=8.5Hz), 3.99 (2H, brs), 3.10-2.90 (2H, m), 2.80-2.59 (2H, m), 2.52-2.20 (1H,m), 2.15-1.90 (1H, m);
TLC : Rf 0.23 (acetic acid:methanol:chloroform=1:2:40).

Example 2(214)

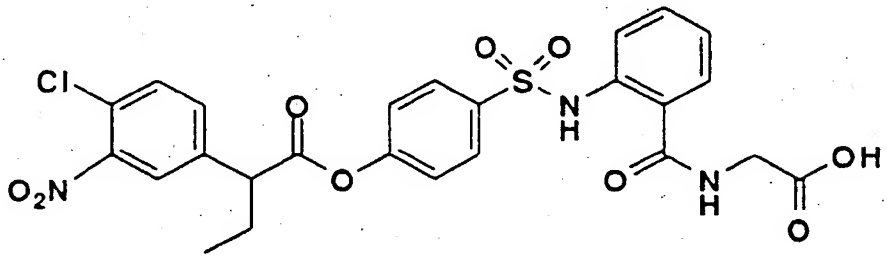
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(3-nitro-4-chlorophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 12.73 (1H, brs), 11.60 (1H, brs), 9.17 (1H, t, J=7Hz), 8.04 (1H, s), 7.90-7.65 (4H, m), 7.55-7.40 (2H, m), 7.35-7.05 (4H, m), 3.90 (2H, d, J=7Hz), 2.90 (2H, m), 2.60 (2H, m), 2.25-1.80 (2H, m);
TLC : Rf 0.34 (acetic acid:methanol:chloroform=1:3:30).

Example 2(215)

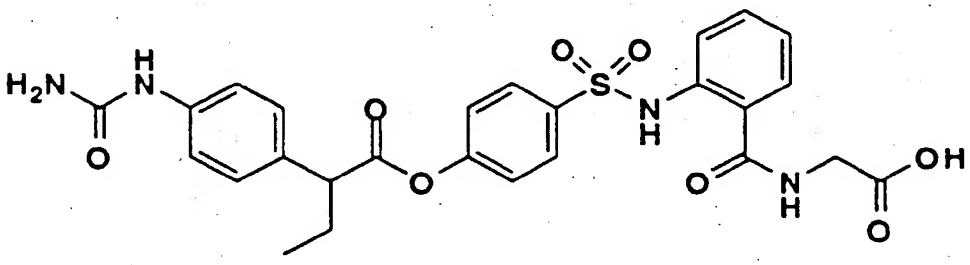
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-chlorophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 10.79 (1H, br), 8.12 (1H, s), 7.85-7.75 (5H, m), 7.28-7.08 (4H, m), 6.74 (1H, t-like), 4.08 (1H, t, J=7.4Hz), 3.84 (2H, d-like), 2.22-2.04 and 1.98-1.76 (each 1H, m), 0.89 (3H, t, J=7.2Hz);
TLC : Rf 0.30 (chloroform:methanol:water=8:2:0.2).

Example 2(216)

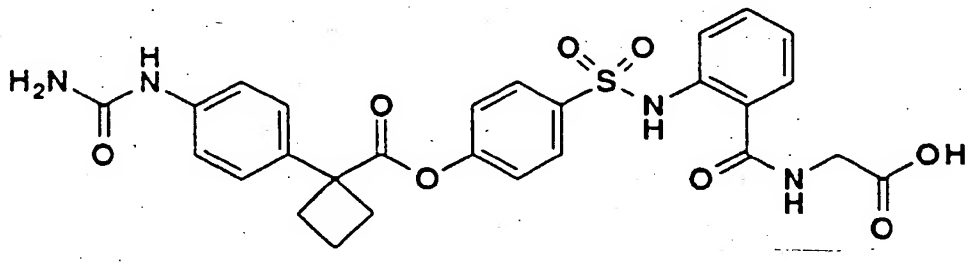
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-ureidophenyl)butanoic acid ester



NMR (DMSO-d_6): δ 10.5 (1H, br), 8.61 (1H, s), 7.81-7.70 (3H, m),7.41-7.05 (10H, m), 6.80 (1H, t, J=7.6Hz), 5.85 (2H, s), 3.84 (2H, s), 3.70 (1H, t, J=7.2Hz), 2.30 (2H, s), 2.60-1.95 and 1.90-1.65 (each 1H, m), 0.88 (3H, t, J=7.0Hz);
TLC : Rf 0.22 (acetic acid:methanol:chloroform=1:3:30).

Example 2(217)

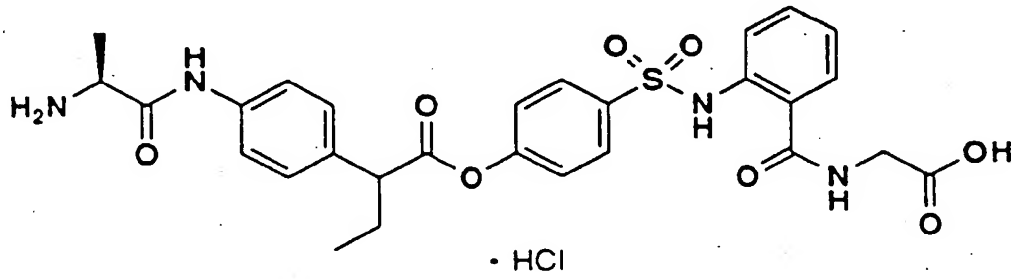
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-ureidophenyl)cyclobutanecarboxylic acid ester



NMR (DMSO-d_6): δ 10.0 (1H, brs), 8.50 (1H, s), 7.67 (4H, d, J=8.8Hz), 7.32-7.09 (2H, m), 7.30 (2H, d, J=8.6Hz), 7.11 (2H, d, J=8.8Hz), 6.96 (2H, d, J=8.6Hz), 6.76 (1H, t, J=6.8Hz), 5.74 (2H, s), 3.75-3.73 (2H, m), 2.80-2.63 (2H, m), 2.53-2.26 (2H, m), 2.23- 2.00 (2H, m);
TLC : Rf 0.10 (chloroform:methanol:acetic acid=40:2:1).

Example 2(218)

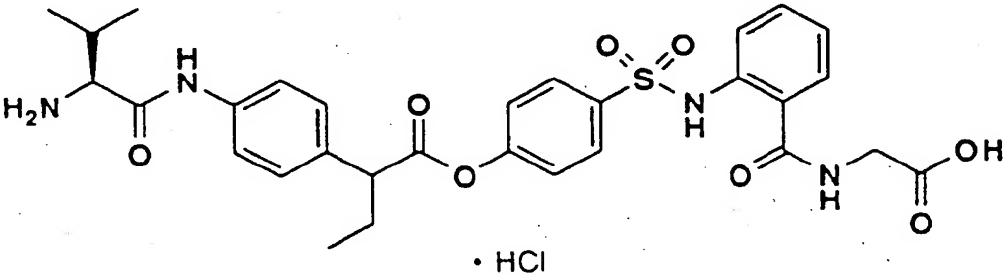
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-(2S-aminopropionyl)amino)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 10.92 (1H, s), 9.47-9.32 (1H, m), 7.85-7.73 (3H, m), 7.66 (2H, d, J=9Hz), 7.54-7.42 (2H, m), 7.34 (2H, d, J=9Hz), 7.27-7.04 (4H, m), 4.16-3.99 (1H, m), 3.89 (2H, d, J=5Hz), 3.81 (1H, t, J=6Hz), 2.19-1.98 and 1.88-1.67 (each 1H, m), 1.47 (3H, d, J=8Hz), 0.97 (3H, t, J=8Hz);
TLC : Rf 0.11 (chloroform:methanol:water=8:2:0.2).

Example 2(219)

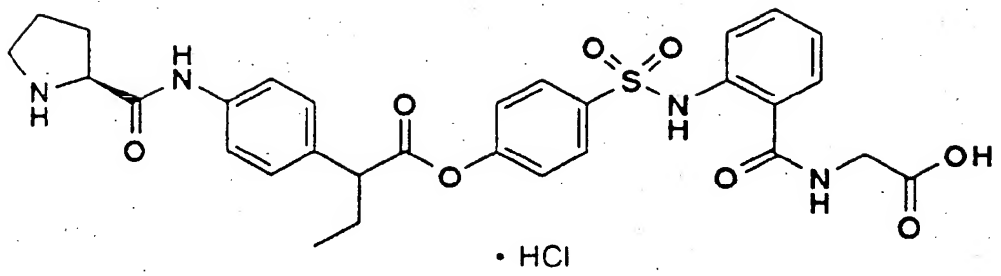
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-(2S-amino-3-methylbutylyl)amino)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 10.96-10.85 (1H, m), 9.45-9.30 (1H, m), 7.85-7.72 (2H, m), 7.66 (2H, d, J=8.4Hz), 7.54-7.42 (2H, m), 7.34 (2H, d, J=8.4Hz), 7.27-7.06 (4H, m), 3.90 (2H, d, J=6.0Hz), 3.81 (1H, t, J=7.8Hz), 2.33-1.98 and 1.92-1.66 (each 1H, m), 1.01 (6H, d, J=7.2Hz), 0.87 (3H, t, J=7.4Hz);
TLC : Rf 0.19 (chloroform:methanol:water=8:2:0.2).

Example 2(220)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-(pyrrolidin-2S-ylcarbonyl)amino)phenyl)butanoic acid ester · hydrochloride

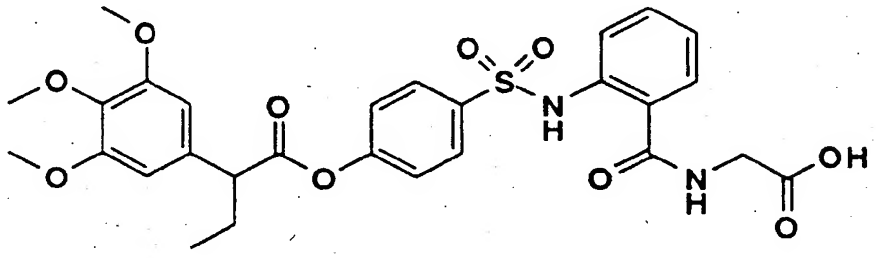


• HCl

NMR (DMSO-d6): δ 10.62-10.52 (1H, m), 9.95-9.70 (1H, m), 7.86-7.70 (3H, m), 7.62 (2H, d, J=8.8Hz), 7.48-7.27 (4H, m), 7.13 (2H, d, J=8.8Hz), 7.04-6.93 (1H, m), 4.34-4.20 (1H, m), 3.95-3.85 (2H, m), 3.81 (1H, t, J=7.1Hz), 3.33-3.16 (2H, m), 2.45-2.21 (1H, m), 2.21-1.68 (5H, m), 0.77 (3H, t, J=7.1Hz);
TLC : Rf 0.09 (chloroform:methanol:water=8:2:0.2).

Example 2(221)

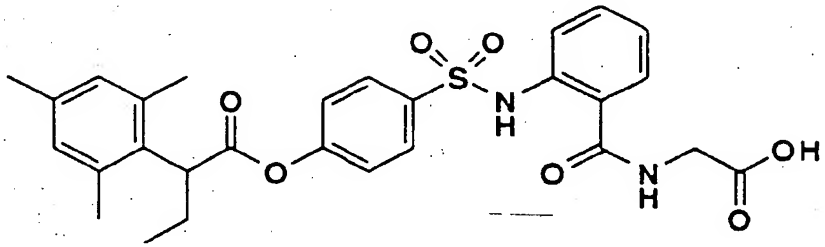
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3,4,5-trimethoxyphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 12.71 (1H, br), 11.69 (1H, br), 9.22 (1H, t-like), 7.80 (2H, d, J=8Hz), 7.73 (1H, d, J=8Hz), 7.53-7.41 (2H, m), 7.25-7.09 (3H, m), 6.63 (2H, s), 3.89 (2H, d, J=5Hz), 3.77 (6H, s), 3.65 (3H, s), 3.63 (1H, t, J=7Hz), 2.19-1.97 and 1.88-1.67 (each 1H, m), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.57 (acetic acid:methanol:chloroform=1:3:30).

Example 2(222)

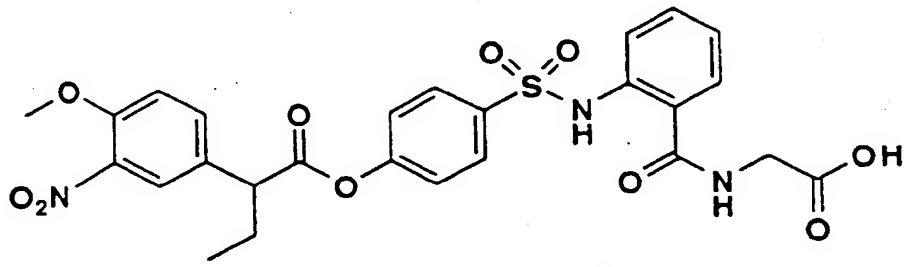
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2,4,6-trimethylphenyl)butanoic acid ester



NMR (CD_3OD): δ 7.80-6.80 (12H, m), 4.21 (1H, dd, J=8.0 and 6.0Hz), 3.93 (2H, s), 2.30-2.20 (each 3H, s), 1.90-1.60 (2H, m), 0.90 (3H, t, J=7.2Hz);
TLC : Rf 0.46 (acetic acid:methanol:chloroform=1:3:30).

Example 2(223)

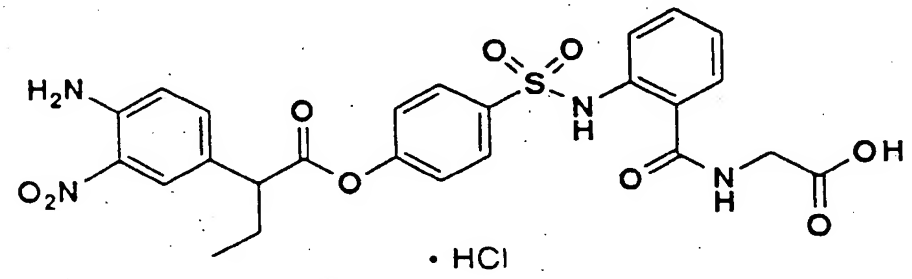
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-methoxyphenyl)butanoic acid ester



NMR (DMSO-d_6): δ 12.72 (1H, br), 11.60 (1H, br), 9.18 (1H, t-like), 7.89-7.59 (5H, m), 7.53-7.46 (2H, m), 7.36 (1H, d, J=9Hz), 7.24 (2H, d, J=9Hz), 7.13 (1H, t, J=8Hz), 3.95 (1H, t, J=8Hz), 3.92 (3H, s), 3.89 (2H, d, J=6Hz), 2.23-2.02 and 1.94-1.72 (each 1H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.51 (acetic acid:methanol:chloroform=1:3:30).

Example 2(224)

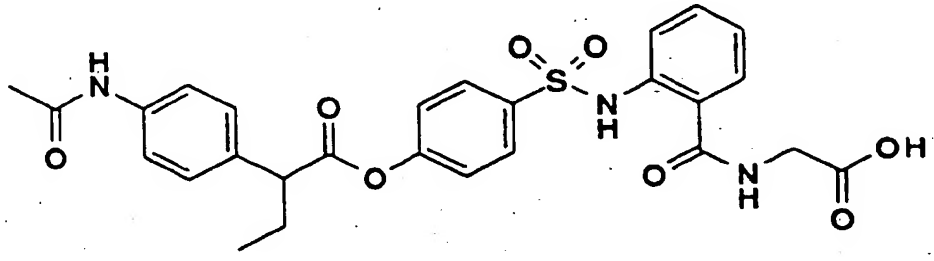
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-aminophenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 12.14 (2H, br), 9.36 (1H, t-like), 7.95 (1H, d, J=2.0Hz), 7.79 (2H, d, J=8.8Hz), 7.76 (1H, d, J=6.6Hz), 7.51-7.38 (5H, m), 7.21 (2H, m), 7.15-7.02 (2H, m), 3.89 (2H, d, J=5.6Hz), 3.80 (1H, t, J=7.6Hz), 2.13-1.99 and 1.84-1.69 (each 1H, m), 0.88 (3H, t, J=7.6Hz);
TLC : Rf 0.18 (chloroform:methanol:water=8:2:0.2).

Example 2(225)

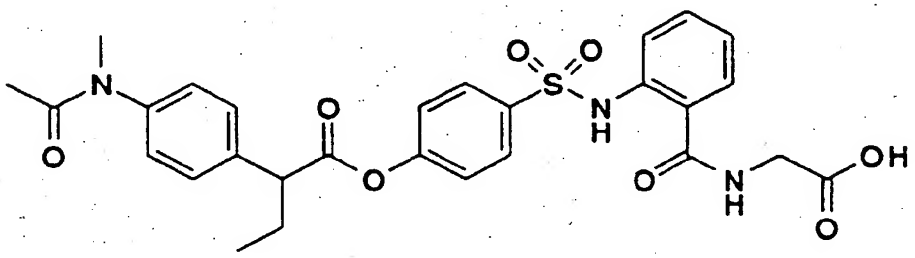
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-acetylamino)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 12.76 (1H, br), 11.58 (1H, s), 9.94 (1H, s), 9.20 (1H, t, J=6Hz), 7.81-7.70 (3H, m), 7.58-7.46 (4H, m), 7.29-7.10 (5H, m), 3.89 (2H, d, J=6Hz), 3.76 (1H, t, J=7Hz), 2.14-1.99 and 1.83-1.69 (each 1H, m), 2.03 (3H, s), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.20 (chloroform:methanol:water=8:2:0.2).

Example 2(226)

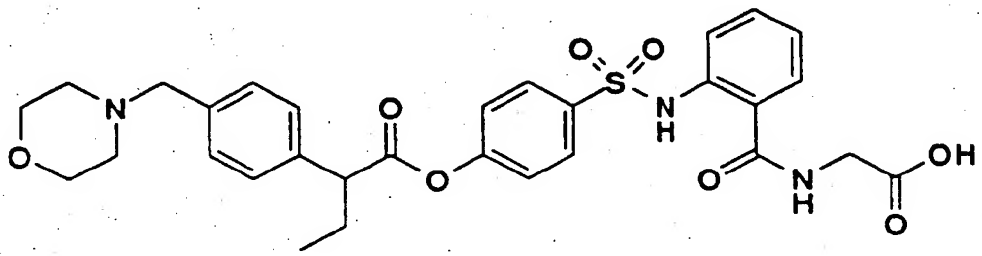
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-methyl-N-acetylamino)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 11.59 (1H, s), 9.19 (1H, t, J=5Hz), 7.80 (2H, d, J=9Hz), 7.73 (1H, d, J=8Hz), 7.53-7.41 (4H, m), 7.34-7.10 (5H, m), 3.89 (2H, d, J=6Hz), 3.69 (1H, t, J=7Hz), 3.16 (3H, s), 2.18-2.01 and 1.92-1.71 (each 1H, m), 1.78 (3H, s), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.27 (chloroform:methanol:water=8:2:0.2).

Example 2(227)

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(morpholin-4-ylmethyl)phenyl)butanoic acid ester · trifluoroacetate

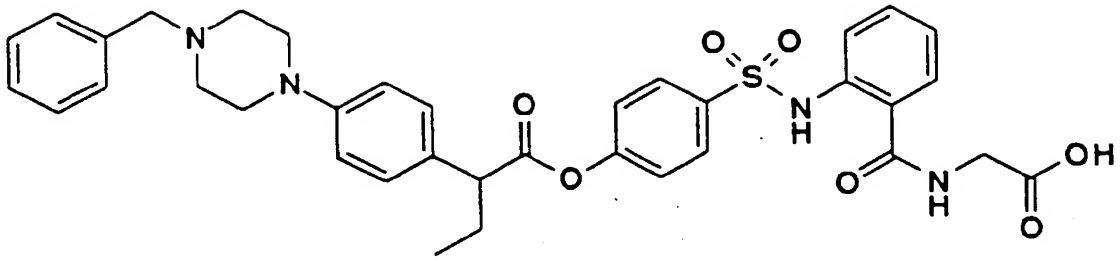


· CF_3COOH

NMR (DMSO-d_6): δ 12.00-11.20 (2H, br), 9.28-9.15 (1H, m), 7.88-7.68 (3H, m), 7.56-7.27 (6H, m), 7.27-7.08 (3H, m), 3.95-3.79 (4H, m), 3.68-3.59 (5H, m), 2.90-2.60 (4H, m), 2.20-1.95 (1H, m), 1.95-1.65 (1H, m), 0.95-0.80 (3H, m);
TLC : Rf 0.47 (acetic acid:methanol;chloroform=1:2:20).

Example 2(228)

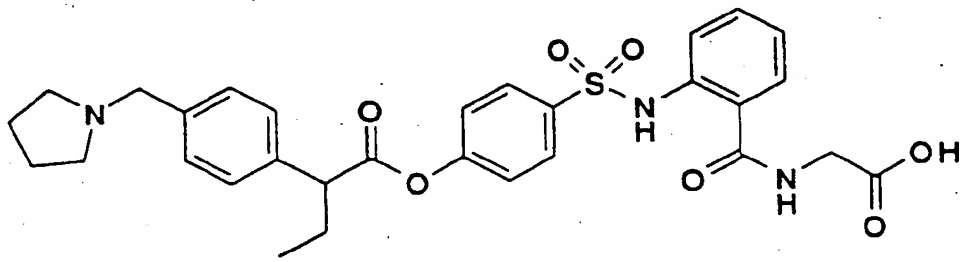
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(4-benzylpiperazin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$+CD_3OD): δ 9.21 (1H, d-like), 7.95-7.86 (4H, m), 7.78-7.71 (1H, m), 7.65-7.58 (2H, m), 7.54-7.46 (6H, m), 7.40-7.32 (2H, m), 7.21-7.10 (2H, m), 3.91 (2H, d, J=7Hz), 3.50-3.06 (11H, m), 1.68-1.45 (2H, m), 0.78 (3H, t, J=7Hz);
TLC : Rf 0.65 (acetic acid:methanol:chloroform=1:3:30).

Example 2(229)

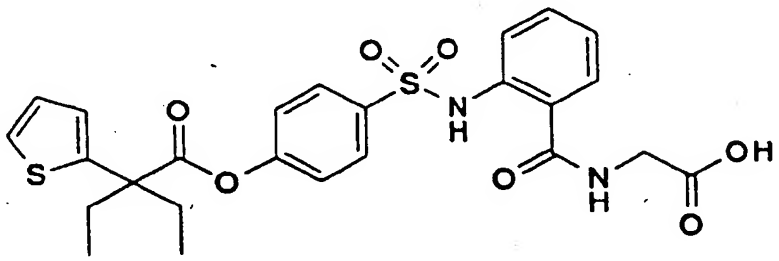
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-ylmethyl)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 9.65 (1H, brs), 7.77 (2H, d, J=8Hz), 7.73 (1H, d, J=8Hz), 7.45-7.30 (6H, m), 7.14 (2H, d, J=8Hz), 6.99 (1H, d, J=8Hz), 4.03-3.93 (2H, m), 3.93-3.80 (3H, m), 2.88 (4H, brs), 2.09 (1H, ddq, J=14Hz, 7Hz, 7Hz), 1.88-1.73 (5H, m), 0.88 (3H, t, J=7Hz);
TLC : Rf 0.10 (acetic acid:methanol:chloroform=1:2:20).

Example 2(230)

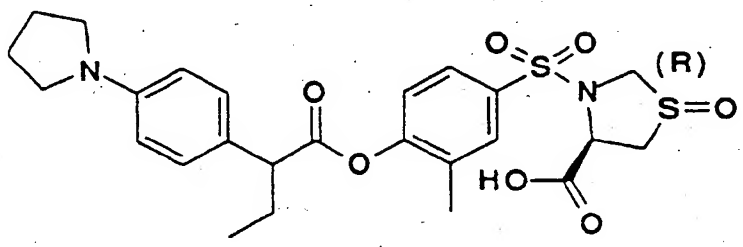
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(thiophen-2-yl)-2-ethylbutanoic acid ester



NMR (DMSO-d_6): δ 9.5-9.3 (1H, brs), 7.9-7.7 (3H, m), 7.5-7.4 (3H, m), 7.3-7.0 (5H, m), 3.87 12H, d, J=5Hz), 2.3-1.9 (4H, m), 0.82 (6H, t, J=7Hz);
TLC : Rf 0.19 (acetic acid:methanol:chloroform=1:2:40).

Example 2(231)

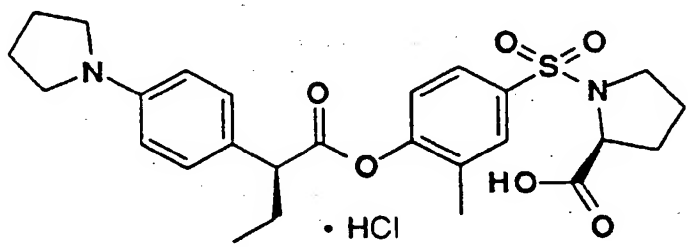
4-((1R-oxo-4S-carboxyperhydrothiazol-3-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 7.85-7.70 (2H, m), 7.18 (2H, d, J=8.5Hz), 7.09 (1H, d, J=8.5Hz),6.53 (2H, d, J=8.5Hz), 4.35-4.65 (2H, m), 4.30 (1H, d, J=12.5Hz), 3.69 (1H, t, J=7.5Hz), 3.35-3.05 (6H, m), 2.20-1.60 (2H, m),1.99 (3H, s), 2.00-1.85 (4H, m), 0.90 (3H, t, J=7.5Hz);
TLC : Rf 0.36 (chloroform:methanol:acetic acid=25:5:1).

Example 2(232)

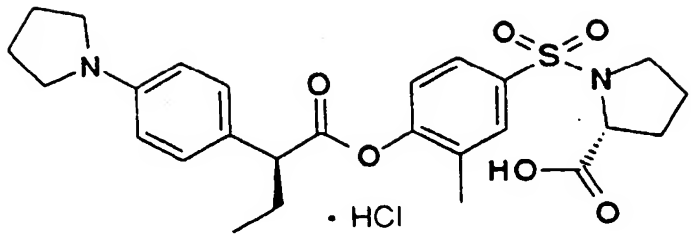
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 7.89-7.69 (2H, m), 7.54 and 7.41 (each 2H, d, J=8Hz), 7.15 (1H, d, J=8Hz), 4.28-4.16 (1H, m), 3.90 (1H, t, J=7Hz), 3.69-3.64 (4H, m), 3.51-3.40 and 3.31-3.21 (each 1H, m), 2.28-2.21 (5H, m), 2.02 (3H, s), 2.01-1.89 (4H, m), 1.80-1.65 (1H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.17 (chloroform:methanol:water=9:1:0.1).

Example 2(233)

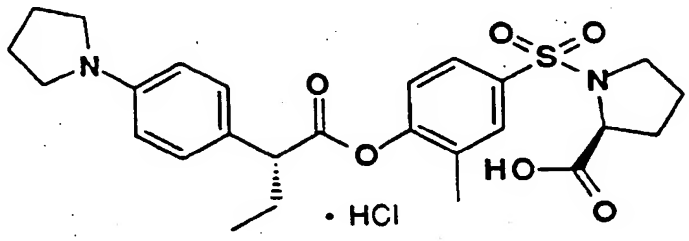
4-((2R-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 7.81-7.68 (2H, m), 7.56 and 7.45 (each 2H, d, J=8Hz), 7.15 (1H, d, J=8Hz), 4.28-4.16 (1H, m), 3.91 (1H, t, J=7Hz), 3.71-3.64 (4H, m), 3.50-3.40 and 3.33-3.22 (each 1H, m), 2.31-2.22 (5H, m), 2.03 (3H, s), 2.02-1.84 (4H, m), 1.80-1.64 (1H, m), 1.00 (3H, t, J=7Hz);
TLC : Rf 0.18 (chloroform:methanol:water=9:1:0.1).

Example 2(234)

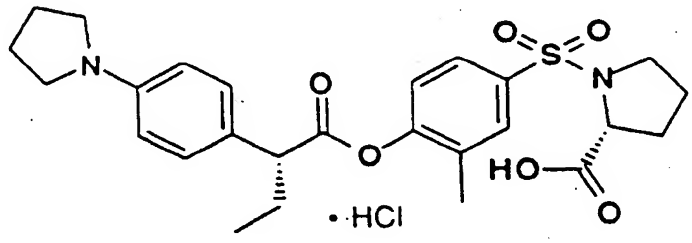
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 7.80-7.68 (2H, m), 7.50 and 7.31 (each 2H, d, J=8Hz), 7.14 (1H, d, J=8Hz), 4.22-4.16 (1H, m), 3.87 (1H, t, J=7Hz), 3.68-3.56 (4H, m), 3.50-3.42 and 3.35-3.20 (each 1H, m), 2.32-2.18 (5H, m), 2.02 (3H, s), 2.01-1.83 (4H, m), 1.79-1.65 (1H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.17 (chloroform:methanol:water=9:1:0.1).

Example 2(235)

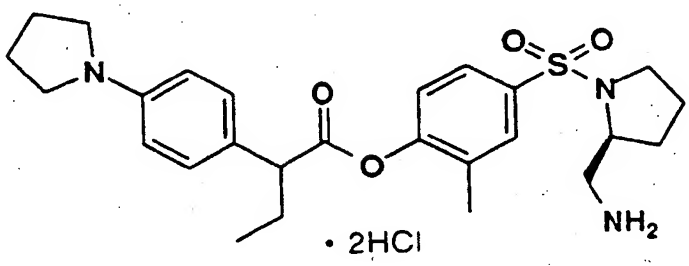
4-((2R-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 7.77-7.68 (2H, m), 7.57 and 7.48 (each 2H, d, J=8Hz), 7.15 (1H, d, J=8Hz), 4.22-4.17 (1H, m), 3.93 (1H, t, J=7Hz), 3.74-3.66 (4H, m), 3.52-3.42 and 3.35-3.21 (each 1H, m), 2.28-2.22 (5H, m), 2.02 (3H, s), 2.01-1.87 (4H, m), 1.80-1.64 (1H, m), 0.99 (3H, t, J=7Hz);
TLC : Rf 0.18 (chloroform:methanol:water=9:1:0.1).

Example 2(236)

4-((2S-aminomethylpyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

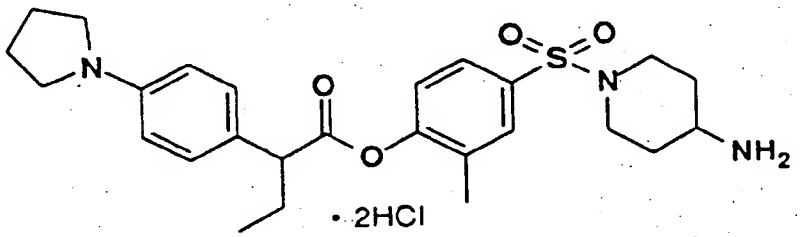


NMR (CD_3OD): δ 7.85-7.70 (2H, m), 7.64 (4H, s), 7.22 (1H, d, J=8.0Hz), 3.98 (1H, t, J=8.0Hz), 4.00-3.80 (1H, m), 3.85-3.70 (4H, m), 3.55-3.20 (2H, m), 3.15-2.95 (2H, m), 2.40-1.80 (2H, m), 2.35-2.25 (4H, m), 2.06 (3H, s), 2.00-1.40 (4H, m), 1.00 (3H, t, J=7.5Hz);

TLC : Rf 0.29 (chloroform:methanol:water=4:1:0.1).

Example 2(237)

4-((4-aminopiperidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-l-yl)phenyl)butanoic acid ester · 2hydrochloride

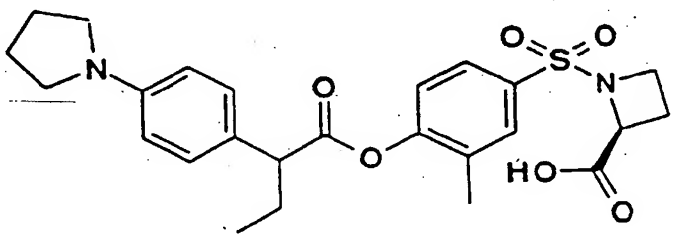


NMR ($DMSO-d_6$): δ 8.14 (2H, brs), 7.63 (1H, s), 7.60 (1H, d, J=8.4Hz), 7.21 (2H, d, J=8.4Hz), 7.20 (1H, d, J=8.4Hz), 6.64 (2H, d, J=8.4Hz), 3.8-3.5 (4H, br), 3.3-3.2 (5H, br), 3.2-3.0 (1H, br), 2.5-2.3 (2H, m), 2.2-2.0 (1H, m), 2.0-1.9 (4H, br), 1.98 (3H, s), 1.9-1.7 (1H, m), 1.7-1.5 (2H, m), 0.90 (3H, t, J=7.2Hz);

TLC : Rf 0.20 (chloroform:methanol=9:1).

Example 2(238)

4-((2S-carboxyazetidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

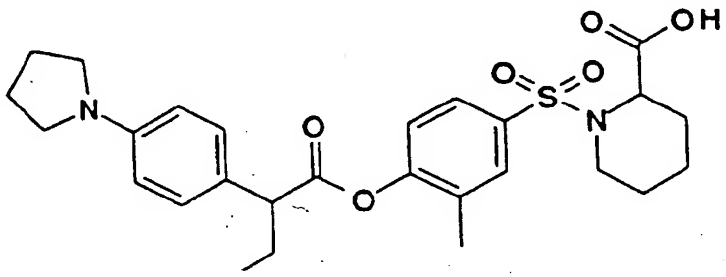


NMR (CD_3OD): δ 7.72 (1H, s), 7.71 (1H, d, J=8.0Hz), 7.22 (2H, d, J=8.8Hz), 7.17 (1H, d, J=8.0Hz), 6.58 (2H, d, J=8.8Hz), 4.30 (1H, t, J=8.5Hz), 3.8-3.6 (3H, m), 3.4-3.2 (4H, m), 2.4-2.1 (3H, m), 2.1-2.0 (4H, brs), 2.0-1.8 (1H, m), 2.04 (3H, s), 1.00 (3H, t, J=7.4Hz);

TLC : Rf 0.59 (chloroform:methanol:acetic acid=25:5:1).

Example 2(239)

4-((2RS-carboxypiperidin-1-yl)sulfonyll-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

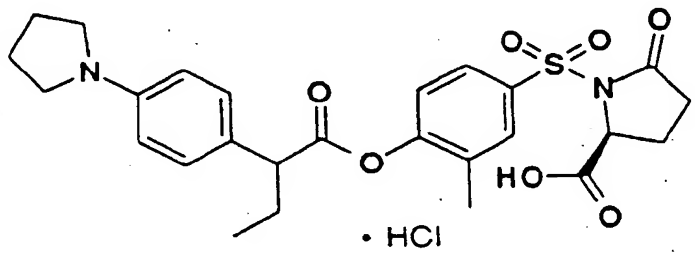


NMR ($CDCl_3$): δ 7.65 (1H, s), 7.63 (1H, d, J=8.2Hz), 7.21 (2H, d, J=8.6Hz), 6.99 (1H, d, J=8.2Hz), 6.53 (2H, d, J=8.6Hz), 4.7-4.6 (1H, brs), 4.7-4.1 (1H, br), 3.59 (1H, t, J=7.7Hz), 3.5-3.2 (6H, brs), 2.3-2.1 (1H, m), 2.1-1.9 (4H, brs), 2.0-1.8 (1H, m), 1.98 (3H, s), 1.6-1.2 (6H, br), 0.96 (3H, t, J=7.4Hz);

TLC : Rf 0.12 (chloroform:methanol=9:1).

Example 2(240)

4-((2-oxo-5S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

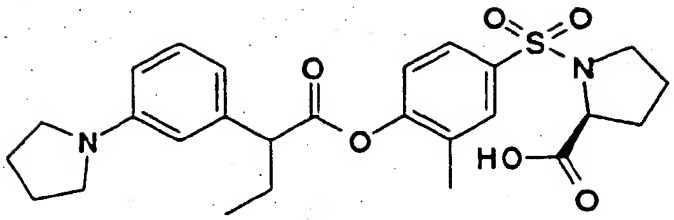


NMR (CD_3OD): δ 7.96-7.82 (2H, m), 7.57 (2H, d, J=8.5Hz), 7.42 (2H, d, J=8.5Hz), 7.13 (1H, d, J=8.0Hz), 4.90-4.80 (1H, m), 3.92 (1H, t, J=7.5Hz), 3.74-3.60 (4H, m), 2.65-1.80 (10H, m), 2.02 (3H, s), 0.99 (3H, t, J=7.5Hz);

TLC : Rf 0.35 (chloroform:methanol:acetic acid=4:1:0.1).

Example 2(241)

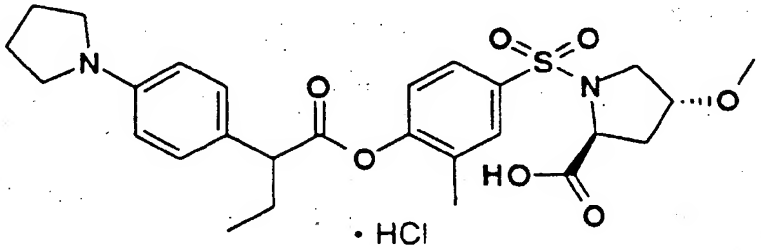
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(3-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70-7.64 (2H, m), 7.20 (1H, t, J=7.8Hz), 7.09 (1H, d, J=7.8Hz), 6.66 (1H, d, J=7.8Hz), 6.53-6.47 (2H, m), 4.3-4.2 (1H, m), 3.8-3.4 (2H, m), 3.4-3.2 (5H, m), 2.3-1.7 (13H, m), 1.01(3H, t, J=7.4Hz);
TLC : Rf 0.58 (chloroform:methanol:acetic acid=9:1:0.2).

Example 2(242)

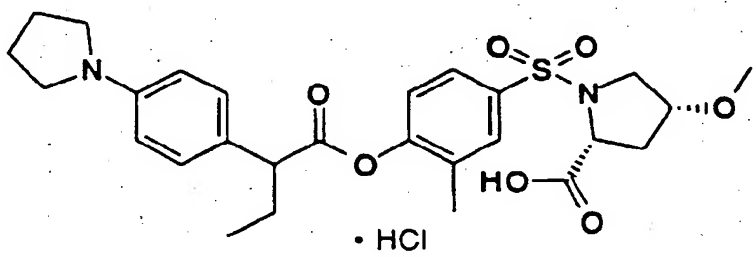
4-((2S-carboxy-4R-methoxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 7.73 (1H, s), 7.66 (1H, d, J=8.6Hz), 7.26 (2H, d, J=8.8Hz), 7.15 (1H, d, J=8.6Hz), 6.78 (2H, d, J=8.8Hz), 5.00 (1H, brs), 4.02 (1H, t, J=7Hz), 3.82 (1H, m), 3.76 (1H, t, J=7Hz), 3.41 (2H, m), 3.31 (4H, m), 2.83 (3H, s), 2.15 (2H, m), 2.00 (4H, m), 1.98 (3H, s), 1.95 (2H, m), 0.92 (3H, t, J=7.4Hz);
TLC : Rf 0.34 (chloroform:methanol:water=4:1:0.1).

Example 2(243)

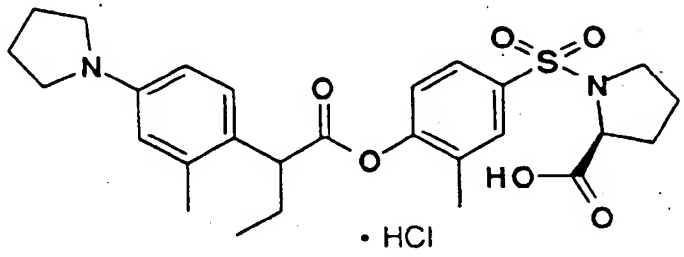
4-((2R-carboxy-4R-methoxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 7.77 (1H, d, J=2.4Hz), 7.70 (1H, dd, J=8.4Hz, 2.4Hz), 7.26 (2H, d, J=8.2Hz), 7.16 (1H, d, J=8.4Hz), 6.75 (2H, d, J=8.2Hz), 4.80 (1H, brs), 4.31 (1H, dd, J=9.2Hz, 3.2Hz), 3.76 (2H, m), 3.33 (6H, m), 3.12 (3H, s), 2.12 (2H, m), 2.02 (4H, m), 1.98 (3H, s), 1.80 (2H, m), 0.91 (3H, t, J=7.2Hz);
TLC : Rf 0.47 (chloroform:methanol:water=4:1:0.1).

Example 2(244)

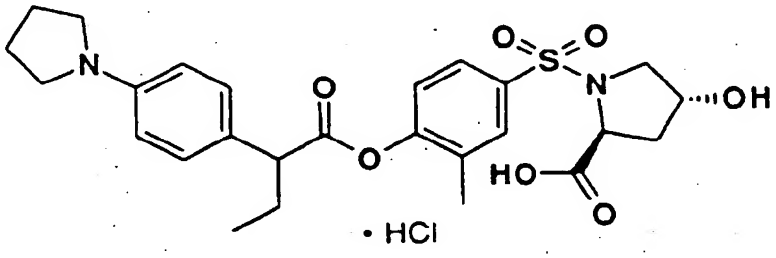
4-((2S-carboxypyrrolidin-1-yl)sulfonyll-2-methylphenyl 2RS-(2-methyl-4-(pyrrolidin-1-yl)phenyl)butanoic acid · ester hydrochloride



NMR (CD_3OD): δ 7.76-7.66 (2H, m), 7.60-7.40 (3H, m), 7.15 (1H, d, J=8.0Hz), 4.30-4.10 (2H, m), 3.85-3.70 (4H, m), 3.55-3.15 (2H, m), 2.57 (3H, s), 2.40-2.15 (5H, m), 2.00 (3H, s), 2.10-1.60 (5H, m), 1.01 (3H, t, J=7.5Hz);
TLC : Rf 0.33 (chloroform:methanol:acetic acid=4:1:0.1).

Example 2(245)

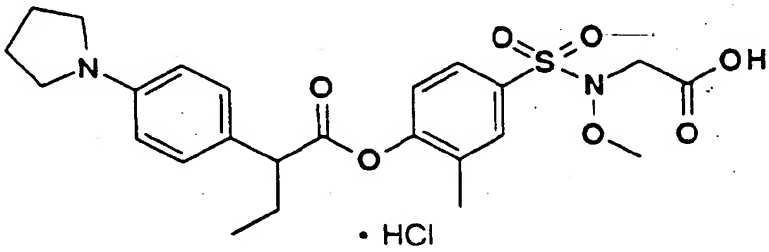
4-((2S-carboxy-4R-hydroxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 7.72 (1H, s), 7.70 (1H, m), 7.20 (2H, d, J=8.6Hz), 7.09 (1H, d, J=8.0Hz), 6.58 (2H, d, J=8.6Hz), 4.32 (1H, m), 4.21 (1H, m), 3.73-3.42 (2H, m), 3.38-3.16 (5H, m), 2,35-1.68 (11H, m), 0.98 (3H, t, J=7.0Hz);
TLC : Rf 0.55 (chloroform:methanol:acetic acid=15:2:1).

Example 2(246)

4-(N-methoxy-N-carboxymethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

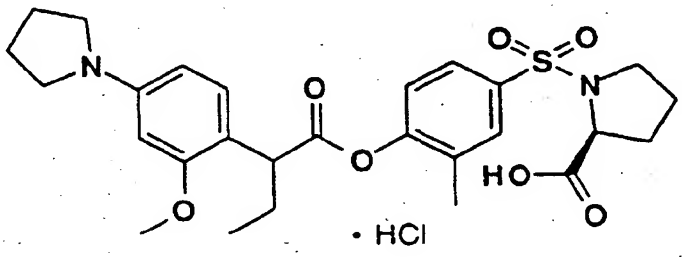


NMR ($CDCl_3$): δ 7.66 (1H, s), 7.63 (1H, d, J=8.0Hz), 7.22 (2H, d, J=8.8Hz), 7.08 (1H, d, J=8.0Hz), 6.54 (2H, d, J=8.8Hz), 5.3-4.6 (1H, br), 3.81 (3H, s), 3.70 (2H, s), 3.69 (1H, t, J=7.8Hz), 3.3-3.2 (4H, brs), 2.2-2.0 (1H, m), 2.1-1.9 (4H, brs), 2.01 (3H, s), 2.0-1.8 (1H, m), 0.97 (3H, t, J=7.4Hz);

TLC : Rf 0.44 (hexane:ethyl acetate=2:1).

Example 2(247)

4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(2-methoxy-4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

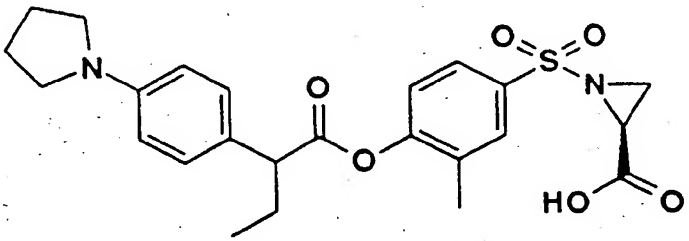


NMR (DMSO-d_6): δ 7.74 (1H, s), 7.68 (1H, d, J=8.5Hz), 7.24-7.06 (2H, m), 6.50-6.30 (2H, m), 4.18-4.06 (1H, m), 4.00 (1H, t, J=7.0Hz), 3.83 (3H, s), 3.40-3.05 (6H, m), 2.20-1.45 (10H, m), 2.05 (3H, s), 0.89 (3H, t, J=7.5Hz);

TLC : Rf 0.40 (chloroform:methanol:acetic acid=4:1:0.11.

Example 2(248)

4-((2S-carboxyaziridin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

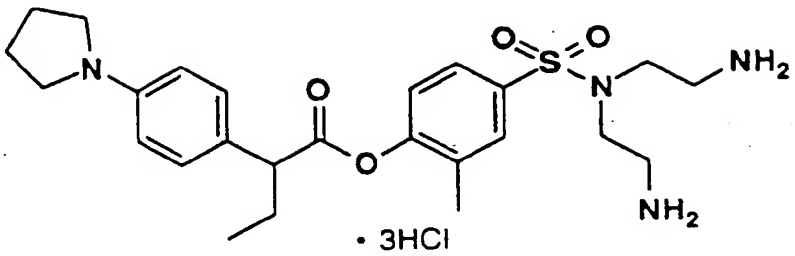


NMR ($CDCl_3$+CD_3OD): δ 7.74 (1H, s), 7.70 (1H, d, J=8.4Hz), 7.20 (2H, d, J=8.4Hz), 7.08 (1H, d, J=8.4Hz), 6.54 (2H, d, J=8.4Hz), 3.61 (1H, t, J=7.5Hz), 3.3-3.2 (4H, brs), 2.6-2.3(3H, brs), 2.3-2.1 (1H, m), 2.1-1.9 (4H, brs), 2.0-1.8 (1H, m), 1.99(3H, s), 0.97 (3H, t, J=7.4Hz);

TLC : Rf 0.28 (chloroform:methanol=4:1).

Example 2(249)

4-(N,N-bis(2-aminoethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 3hydrochloride

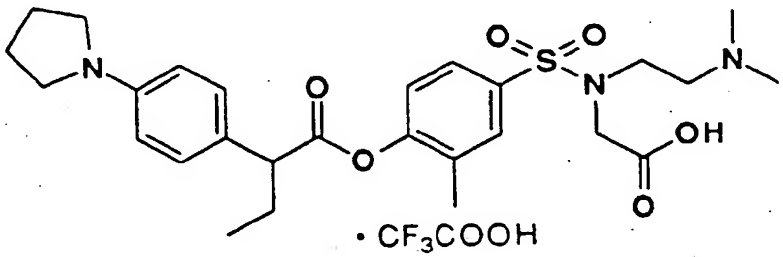


NMR (DMSO-d_6): δ 8.25 (4H, m), 7.80 (1H, d, J=1.0Hz), 7.71 (1H, dd, J=8.6Hz, 1.0Hz), 7.26 (3H, m), 6.82 (2H, m), 3.78 (1H, t, J=7.8Hz), 3.35 (8H, m), 3.04 (4H, m), 2.13 (1H, m), 2.02 (3H, s), 1.98 (4H, m), 1.85 (1H, m), 0.92 (3H, t, J=7.2Hz);

TLC : Rf 0.31 (chloroform:methanol:water=6:4:1).

Example 2(250)

4-(N-carboxymethyl-N-(2-(N',N'-dimethylamino)ethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · trifluoroacetate

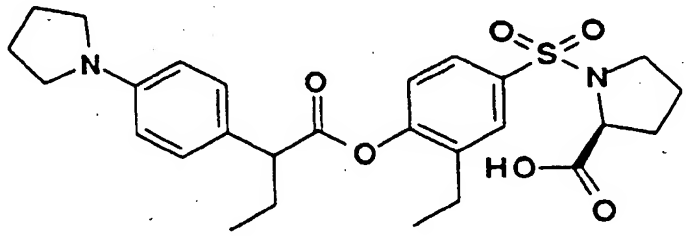


NMR ($CDCl_3$): δ 7.61-7.55 (2H, m), 7.21 (2H, d, J=8.7Hz), 7.07 (1H, d, J=8.2Hz), 6.54 (2H, d, J=8.7Hz), 3.80 (2H, s), 3.60 (1H, t, J=7.8Hz), 3.55-3.10 (8H, m), 2.83 (6H, s), 2.30-1.70 (9H, m), 0.98 (3H, t, J=7.4Hz);

TLC : Rf 0.43 (chloroform:methanol:water=8:2:0.2).

Example 2(251)

4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-ethylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester

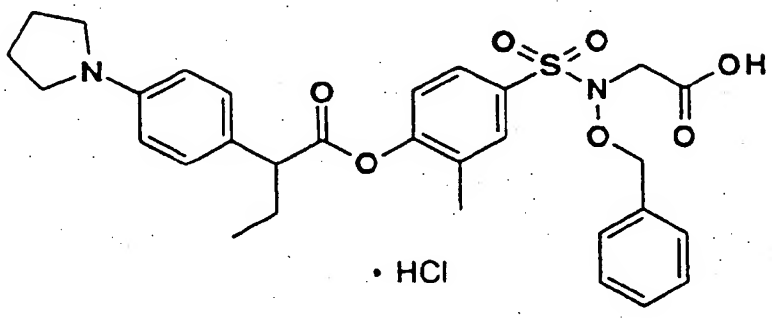


NMR ($CDCl_3$): δ 7.8-7.6 (m, 2H), 7.36 (d, J=8.4Hz, 2H), 7.07 (d, J=8.4Hz, 1H), 7.02 (d, J=8.4Hz, 2H), 4.3-4.2 (m, 1H), 3.70 (t, J=7.2Hz, 1H), 3.6-3.4 (m, 5H), 3.3-3.1 (m, 1H), 2.37 (q, J=7.6Hz, 2H), 2.3-1.6 (m, 10H), 1.03 (t, J=7.6Hz, 3H), 0.99 (t, J=7.6Hz, 3H);

TLC : Rf 0.33 (chloroform:methanol:acetic acid=50:2:1).

Example 2(252)

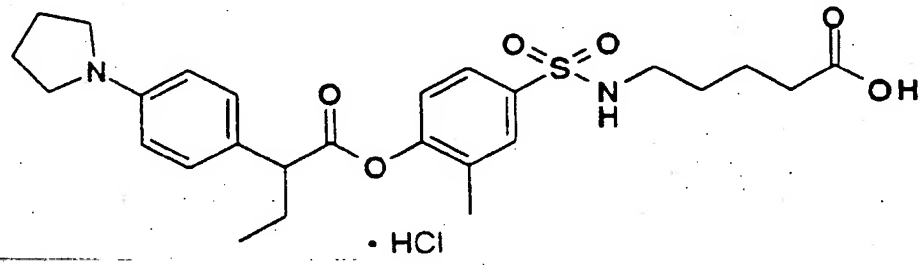
4-(N-carboxymethyl-N-benzyloxyaminosulfonyll-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 7.70 (1H, s), 7.68 (1H, d, J=8.6Hz), 7.32 (5H, s), 7.20 (2H, d, J=8.2Hz), 7.16 (1H, d, J=8.6Hz), 6.52 (2H, d, J=8.2Hz), 5.25 (2H, s), 3.8-3.4 (2H, m), 3.5-3.4 (2H, brs), 3.3-3.1 (4H, brs), 2.2-2.0 (1H, m), 2.0-1.8 (4H, brs), 1.9-1.7 (1H, m), 1.93(3H, s), 0.89 (3H, t, J=7.2Hz);
TLC : Rf 0.29 (chloroform:methanol=9:1).

Example 2(253)

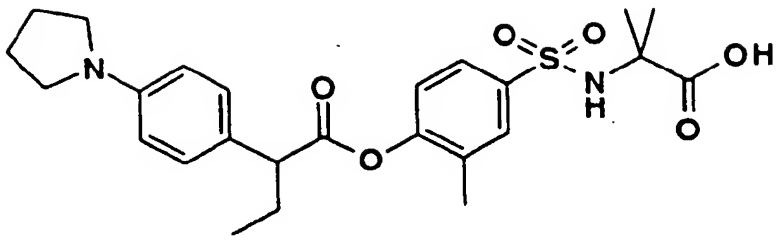
4-(N-(4-carboxybutyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6 + 2 drops of D2O): δ 7.66 (1H, s-like), 7.63 (1H, dd, J=2 and 8Hz), 7.24 (2H, d, J=8Hz), 7.14 (2H, d, J=8Hz), 6.69 (2H, d, J=8Hz), 3.74 (1H, t, J=7Hz), 3.31-3.25 (4H, m), 2.71 (2H, t, J=7Hz), 2.18-1.72 (2H, m), 2.15 (2H, t, J=7Hz), 2.01-1.94 (4H, m), 1.96 (3H, s), 1.53-1.34 (4H, m), 0.91 (3H, t, J=7Hz);
TLC : Rf 0.38 (chloroform:methanol:water=9:1:0.1).

Example 2(254)

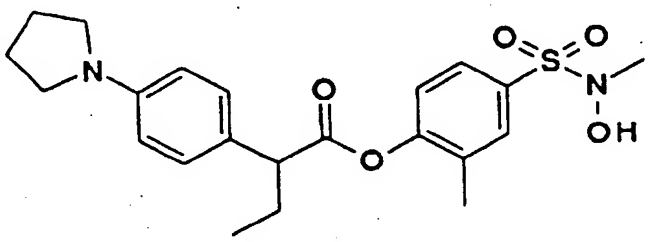
4-(N-(1,1-dimethyl-1-carboxymethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (DMSO-d_6): δ 7.68 (1H, s-like), 7.64 (1H, dd, J=2 and 8Hz), 7.39 (1H, br), 7.18 (2H, d, J=8Hz), 7.07 (1H, d J=8Hz), 6.53 (2H, d, J=8Hz), 3.69 (1H, t, J=7Hz), 3.24-3.18 (4H, m), 2.20-1.65 (2H, m), 1.98-1.91 (4H, m), 1.93 (3H, s) 1 18 (6H, s), 0.90 (3H, t, J=7Hz);
TLC : Rf 0.19 (chloroform:methanol:water=9:1:0.1).

Example 2(255)

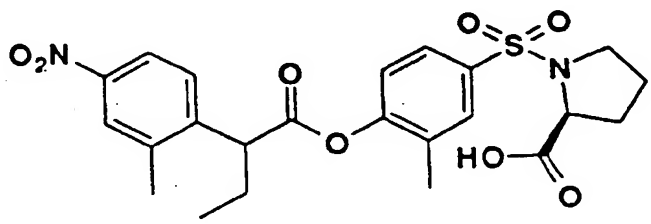
4-(N-methyl-N-hydroxyaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.71 (1H, s), 7.69 (1H, d, J=8.6Hz), 7.23 (2H, d, J=8.8Hz), 7.13 (1H, d, J=8.6Hzl, 6.55 (2H, d, J=8.8Hz), 6.54 (1H, s), 3.63 (1H, t, J=7.7Hz), 3.3-3.2 (4H, brs), 2.81 (3H, s), 2.3-2.1 (1H, m), 2.1-1.9 (4H, brs), 2.06 (3H, s), 2.0-1.8 (1H, m), 0.99 (3H, t, J=7.3Hz);
TLC : Rf 0.43 (hexane:ethyl acetate=2:1).

Example 2(256)

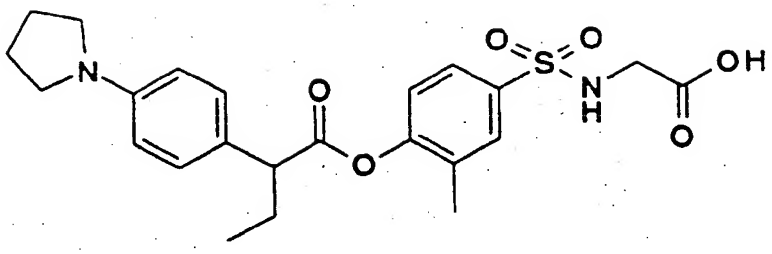
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(2-methyl-4-nitrophenyl)butanoic acid ester



NMR ($CDCl_3$): δ 8.15-8.05 (2H, m), 7.75-7.65 (2H, m), 7.56 (1H, d, J=8.0Hz), 7.09 (1H, d, J=9.0Hz), 4.25 (1H, dd, J=3.5, 7.0Hz), 4.13 (1H, t, J=7.5Hz), 3.60-3.40 (1H, m), 3.30-3.10 (1H, m), 2.59 (3H, s), 2.45-1.60 (6H, m), 1.99 (3H, s), 1.02 (3H, t, J=7.5Hz);
TLC : Rf 0.24 (chloroform:methanol:water=9:1:0.1).

Example 2(257)

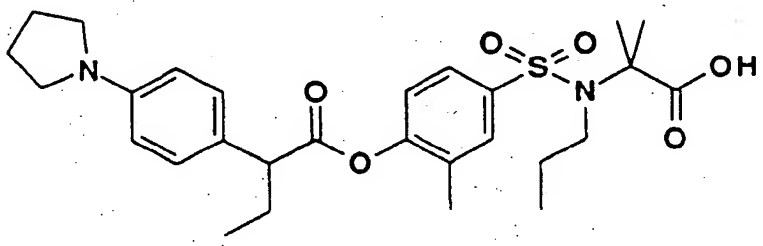
4-(N-carboxymethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70-7.58 (2H, m), 7.25 (2H, d, J=8Hz), 7.01 (1H, d, J=8Hz), 6.65 (2H, d, J=8Hz), 5.43-5.23 (1H, br), 5.18-4.80 (1H, br), 3.75 (2H, brs), 3.63 (1H, t, J=7Hz), 3.40-3.20 (4H, m), 2.28-1.80 (9H, m), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(258)

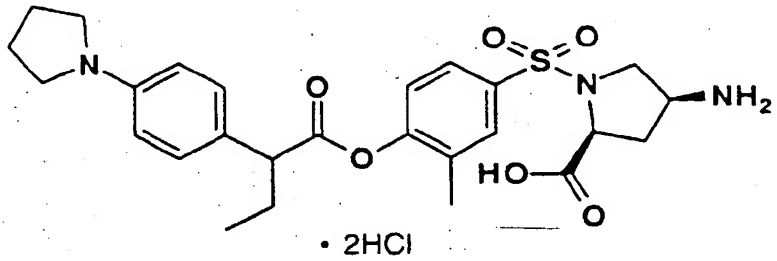
4-(N-(1,1-dimethyl-1-carboxymethyl)-N-propylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR (DMSO-d_6 + 2 drops of D2O): δ 7.80 (1H, s-like), 7.78 (1H, dd, J=2 and 8Hz), 7.18 (2H, d, J=8Hz), 7.11 (1H, d, J=8Hz), 6.54 (2H, d, J=8Hz), 3.70 (1H, t, J=7Hz), 3.25-3.17 (4H, m), 3.12-3.04 (2H, m), 2.20-1.70 (2H, m), 1.99-1.92 (4H, m), 1.95 (3H, s), 1.57-1.42 (2H, m), 1.45 (6H, s), 0.91 (3H, t, J=7Hz), 0.71 (3H, t, J=7Hz);
TLC : Rf 0.57 (chloroform:methanol:water=9:1:0.1).

Example 2(259)

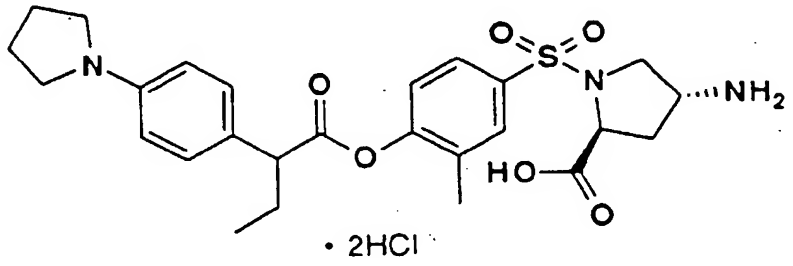
4-((2S-carboxy-4S-aminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (CD_3OD): δ 7.83-7.68 (2H, m), 7.63 (4H, s-like), 7.22 (1H, d, J=8.2Hz), 4.21 (1H, dd, J=9.2 and 3.4Hz), 3.98 (1H, t, J=7.8Hz), 3.90-3.43 (7H, m), 2.70-1.84 (8H, m), 2.06 (3H, s), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.46 (ethyl acetate:acetic acid:water=6:2:1).

Example 2(260)

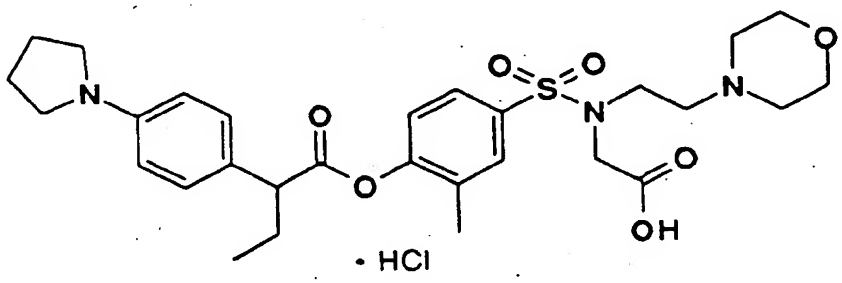
4-((2S-carboxy-4R-aminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (CD_3OD): δ 7.84-7.68 (2H, m), 7.63 (4H, s-like), 7.18 (1H, d, J=8.0Hz), 4.55 (1H, dd, J=8.4 and 4.2Hz), 4.07-3.90 (2H, m), 3.90-3.63 (5H, m), 3.47-3.26 (1H, m), 2.53-1.82 (8H, m), 2.05 (3H, s), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.42 (ethyl acetate:acetic acid:water=6:2:1).

Example 2(261)

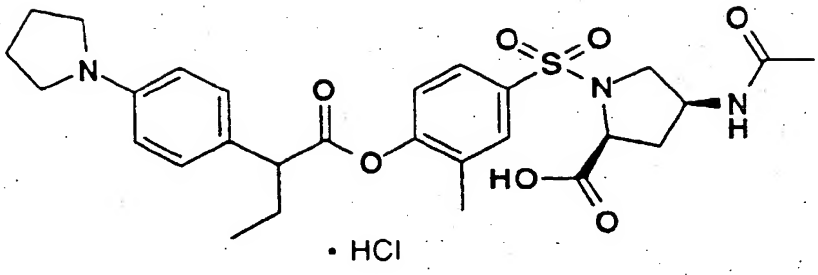
4-(N-carboxymethyl-N-(2-(morpholin-4-yl)ethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR ($CDCl_3$): δ 7.66-7.52 (2H, m), 7.21 (2H, d, J=8.5Hz), 7.09 (1H, d, J=8.5Hz), 6.55 (2H, d, J=8.5Hz), 3.95-3.80 (4H, m), 3.75 (2H, s), 3.61 (1H, t, J=7.5Hz), 3.45-3.20 (6H, m), 3.10-2.70 (6H, m), 2.30-1.75 (6H, m), 2.04 (3H, s), 0.99 (3H, t, J=7.5Hz);
TLC : Rf 0.24 (chloroform:methanol:water=9:1:0.1).

Example 2(262)

4-((2S-carboxy-4S-acetylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



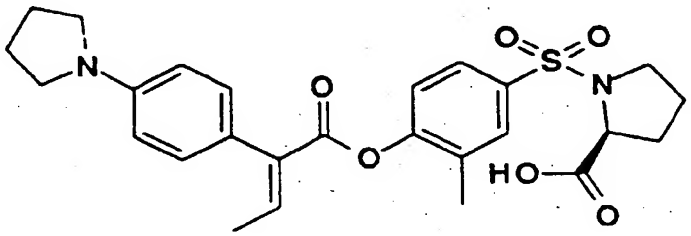
• HCl

NMR (DMSO-d_6): δ 8.02 (1H, d, J=7.8Hz), 7.74 (1H, d, J=2.2Hz), 6.69 (1H, dd, J=8.4Hz, 2.2Hz), 7.17 (2H, d, J=8.6Hz), 7.17 (1H, d, J=8.4Hz), 6.54 (2H, d, J=8.6Hz), 4.13 (1H, t, J=7.8Hz), 3.82 (1H, m), 3.70 (1H, t, J=7.6Hz), 3.50 (1H, m), 3.22 (4H, m), 3.06 (1H, m), 2.31 (1H, m), 2.07 (1H, m), 1.99 (3H, s), 1.96 (4H, m), 1.82 (2H, m), 1.75 (3H, s), 0.91 (3H, t, J=7.4Hz);

TLC : Rf 0.18 (chloroform:methanol:water=4:1:0.1).

Example 2(263)

4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)-2-butenic acid ester

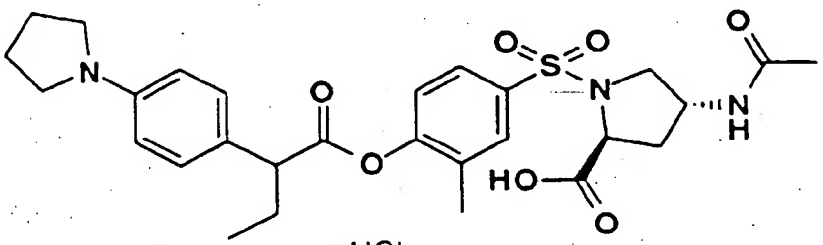


NMR ($CDCl_3$): δ 7.80-7.65 (2H, m), 7.32 (1H, q, J=7Hz), 7.23 (1H, d, J=8Hz), 7.13 (2H, d, J=8Hz), 6.59 (2H, d, J=8Hz), 4.30-4.20 (1H, m), 4.10-3.60 (1H, b), 3.60-3.45 (1H, m), 3.40-3.20 (5H, m), 2.30-1.65 (8H, m), 2.25 (3H, s), 1.88 (3H, d, J=7Hz);

TLC : Rf 0.28 (chloroform:methanol:acetic acid=4:2:0.1).

Example 2(264)

4-((2S-carboxy-4R-acetylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride

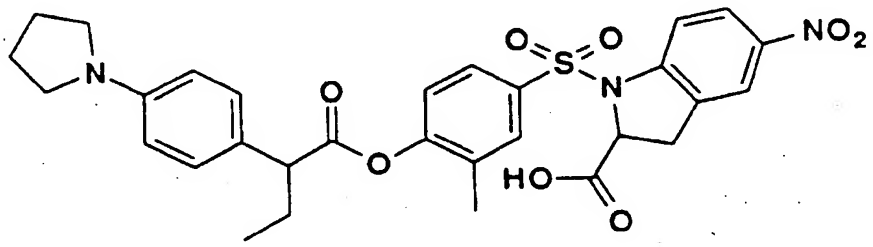


• HCl

NMR (DMSO-d_6): δ 7.78 (1H, d, J=5Hz), 7.68 (1H, s), 7.64 (1H, d, J=8.0Hz), 7.19 (2H, d, J=8.6Hz), 7.16 (1H, d, J=8.0Hz), 6.56 (2H, d, J=8.6Hz), 4.28 (1H, t, J=7.8Hz), 4.12 (1H, m), 3.75 (1H, m), 3.48 (1H, m), 3.23 (4H, m), 3.06 (1H, m), 2.12 (1H, m), 2.03 (2H, m), 1.99 (3H, s), 1.96 (4H, m), 1.80 (1H, m), 1.54 (3H, s), 0.91 (3H, t, J=7.2Hz);
TLC : Rf 0.19 (chloroform:methanol:water=4:1:0.1).

Example 2(265)

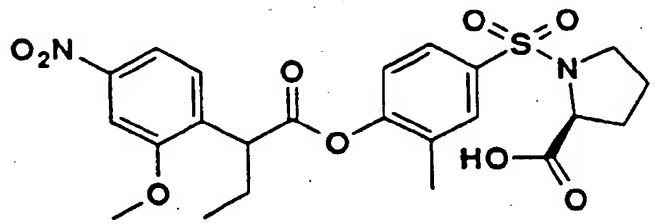
4-((2RS-carboxy-5-nitroindolin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 8.33 (1H, d, J=2Hz), 7.89 (1H, dd, J=8, 2Hz), 7.67 (1H, s), 7.62 (1H, d, J=8Hz), 7.20 (1H, d, J=8Hz), 7.18 (2H, d, J=8Hz), 7.02 (1H, d, J=8Hz), 6.55 (2H, d, J=8Hz), 4.85 (1H, dd, J=10, 5Hz), 4.60-4.25 (1H, br), 3.59 (1H, t, J=7Hz), 3.40-3.15 (6H, m), 2.25-1.75 (9H, m), 0.95 (3H, t, J=7Hz);
TLC : Rf 0.30 (chloroform:methanol:acetic acid=4:2:0.1).

Example 2(266)

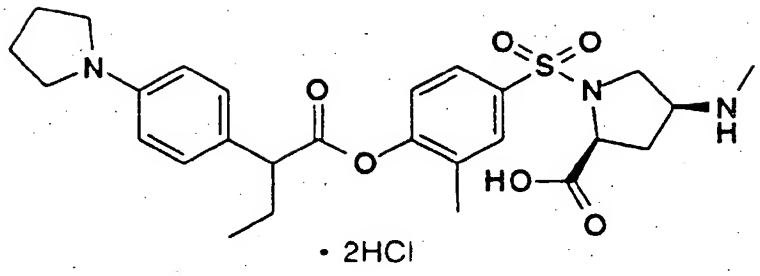
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(2-methoxy-4-nitrophenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.88 (1H, dd, J=2.0, 8.5Hz), 7.78 (1H, d, J=2.0Hz), 7.75-7.65 (2H, m), 7.49 (1H, d, J=8.5Hz), 7.12 (1H, d, J=9.0Hz), 4.30-4.15 (2H, m),3.98 (3H, s),3.60-3.40 (1H, m),3.30-3.10 (1H, m),2.40-1.60 (6H, m), 2.08 (3H, s), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.38 (chloroform:methanol:acetic acid=4:2:0.1).

Example 2(267)

4-((2S-carboxy-4S-methylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



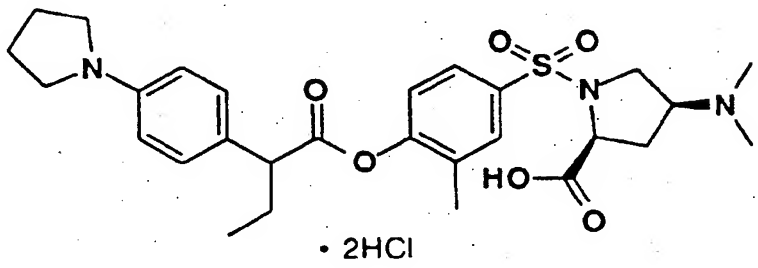
• 2HCl

NMR (CD_3OD): δ 7.77 (1H, s), 7.75 (1H, d, J=8.0Hz), 7.37 (2H, d, J=8.6Hz), 7.19 (1H, d, J=8.0Hz), 6.98 (2H, d, J=8.6Hz), 4.18 (1H, m), 3.69 (3H, m), 3.59 (1H, m), 3.46 (4H, m), 2.72 (3H, s), 2.57 (1H, m), 2.21 (2H, m), 2.13 (4H, m), 2.02 (3H, s), 1.93 (1H, m), 0.98 (3H, t, J=7.4Hz);

TLC : Rf 0.28 (chloroform:methanol:water=4:1:0.1).

Example 2(268)

4-((2S-carboxy-4S-(N,N-dimethylamino)pyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl) butanoic acid ester · 2hydrochloride



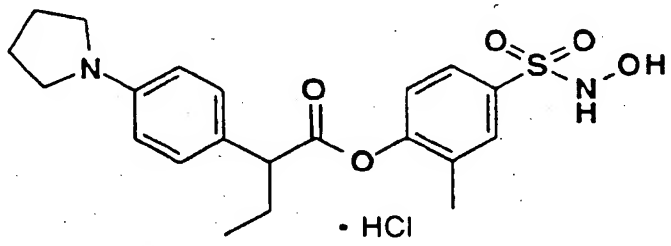
• 2HCl

NMR (CD_3OD): δ 7.81 (1H, s), 7.78 (1H, d, J=8.2Hz), 7.62 (4H, s), 7.21 (1H, d, J=8.2Hz), 4.25 (1H, t, J=7Hz), 3.98 (1H, t, J=7Hz), 3.77 (4H, m), 3.65 (3H, m), 2.90 (6H, s), 2.80 (1H, m), 2.29 (4H, m), 2.24 (2H, m), 2.06 (3H, s), 1.99 (1H, m), 1.00 (3H, t, J=7.4Hz);

TLC : Rf 0.42 (chloroform:methanol:water=6:4:1).

Example 2(269)

4-(N-hydroxyaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



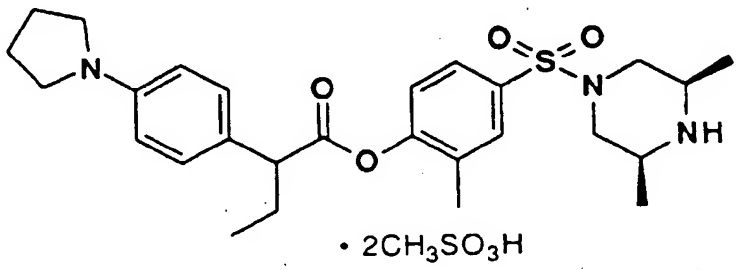
• HCl

NMR ($CDCl_3$): δ 7.73 (1H, s), 7.68 (1H, d, J=8.6Hz), 7.23 (2H, d, J=8.0Hz), 7.2-7.0 (2H, br), 7.04 (1H, d, J=8.6Hz), 6.63 (2H, d, J=8.0Hz), 3.63 (1H, t, J=7.7Hz), 3.4-3.2 (4H, brs), 2.3-2.1 (1H, m), 2.1-1.9 (4H, brs), 2.00 (3H, s), 2.0-1.8

(1H, m), 0.97 (3H, t, J=7.3Hz);
TLC : Rf 0.25 (hexane:ethyl acetate=2:1).

Example 2(270)

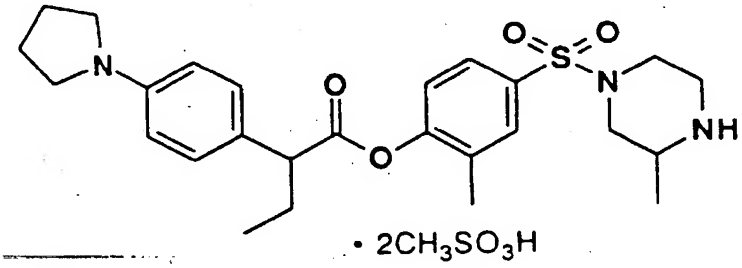
4-((2S,6S-dimethylpiperazin-4-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2methanesulfonic acid salt



NMR ($CDCl_3$): δ 7.76-7.62 (6H, m), 7.23 (1H, d, J=8.5Hz), 4.01 (1H, t, J=7.5Hz), 4.00-3.75 (6H, m), 3.55-3.30 (2H, m), 2.68 (6H, s), 2.45-1.80 (8H, m), 2.07 (3H, s), 1.31 (6H, d, J=6.5Hz), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.66 (chloroform:methanol:water=4:1:0.1).

Example 2(271)

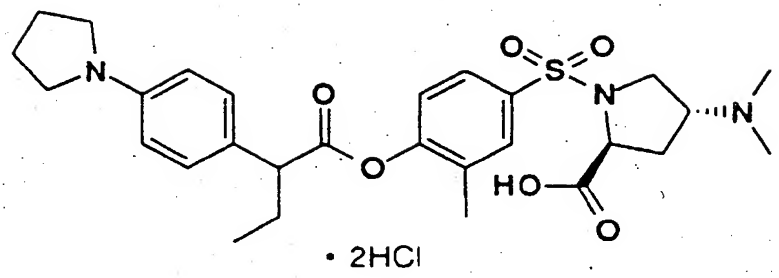
4-((2RS-methylpiperazin-4-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2methanesulfonic acid salt



NMR ($CDCl_3$): δ 7.76-7.60 (6H, m), 7.23 (1H, d, J=8.0Hz), 4.01 (1H, t, J=7.5Hz), 3.90-3.72 (6H, m), 3.55-3.35 (2H, m), 3.32-3.13 (1H, m), 2.82-2.62 (1H, m), 2.67 (6H, s), 2.49 (1H, dd, J=13.0, 10.0Hz), 2.40-1.80 (6H, m), 2.07 (3H, s), 1.32 (3H, d, J=6.5Hz), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.45 (chloroform:methanol:water=9:1:0.1).

Example 2(272)

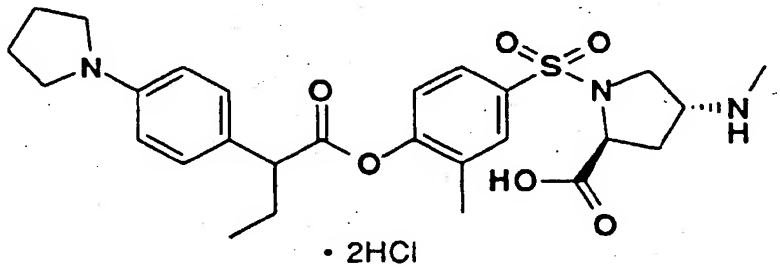
4-((2S-carboxy-4R-(N,N-dimethylamino)pyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl) butanoic acid ester · 2hydrochloride



NMR (DMSO-d_6): δ 11.38 (1H, m), 7.77 (1H, s), 7.72 (1H, d, J=8.2Hz), 7.19 (3H, m), 6.63 (2H, d, J=8.6Hz), 4.38 (1H, m), 4.01 (1H, m), 3.82 (1H, m), 3.73 (1H, t, J=7.4Hz), 3.49 (1H, t, J=8.6Hz), 3.24 (4H, m), 2.70 (6H, s), 2.36 (2H, ml, 2.11 (1H, ml, 1.99 (3H, s), 1.97 (4H, m), 1.83 (1H, ml, 0.91 (3H, t, J=7.2Hz);
TLC : Rf 0.44 (chloroform:methanol:water=6:4:1).

Example 2(273)

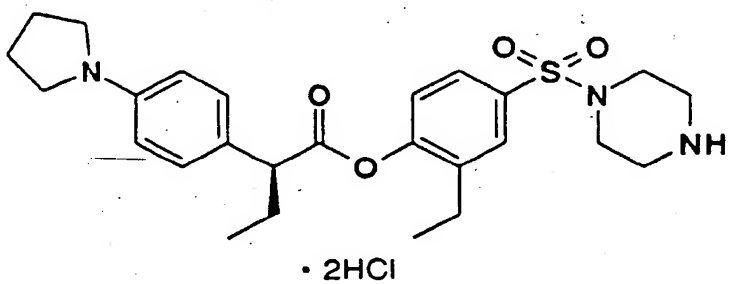
4-((2S-carboxy-4R-methylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (CD_3OD): δ 7.76 (1H, s), 7.73 (1H, d, J=8.0Hz), 7.25 (2H, d, J=8.4Hz), 7.13 (1H, d, J=8.0Hz), 6.71 (2H, d, J=8.4Hz), 4.53 (1H, m), 3.97 (1H, m), 3.86 (1H, m), 3.70 (1H, t, J=8Hz), 3.41 (1H, m), 3.35 (4H, m), 2.70 (3H, s), 2.49 (1H, m), 2.31 (1H, m), 2.17 (1H, m), 2.06 (4H, m), 2.00 (3H, s), 1.92 (1H, m), 0.98 (3H, t, J=7.2Hz);
TLC : Rf 0.46 (chloroform:methanol:water=6:4:1).

Example 2(274)

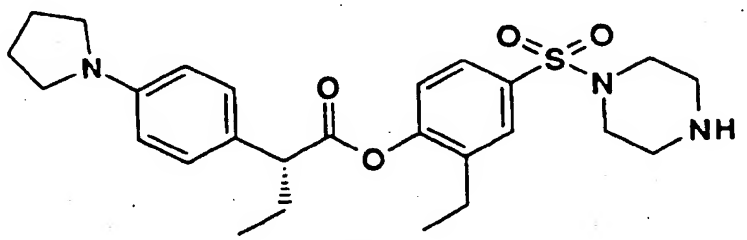
4-(piperazin-4-ylsulfonyl)-2-ethylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride



NMR (CD_3OD): δ 7.75-7.50 (6H, m), 7.25 (1H, d, J=9.0Hz), 3.97 (1H, t, J=7.5Hz), 3.85-3.70 (4H, m), 3.35-3.15 (8H, m), 2.50-1.80 (8H, m), 1.00 (6H, t, J=7.5Hz);
TLC : Rf 0.46 (chloroform:methanol:water=9:1:0.1).

Example 2(275)

4-(piperazin-4-ylsulfonyl)-2-ethylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

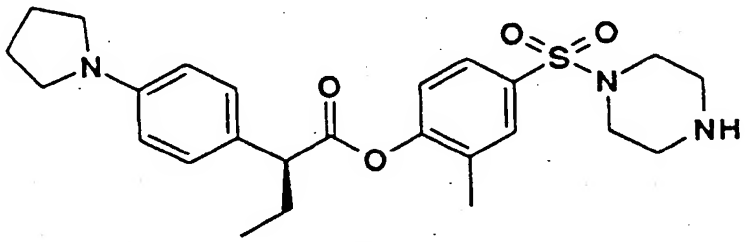


• 2HCl

NMR (CD_3OD): δ7.75-7.58 (6H, m), 7.25 (1H, d, J=9.0Hz), 3.98 (1H, t, J=7.5Hz), 3.90-3.70 (4H, m), 3.40-3.20 (8H, m), 2.50-1.80 (8H, m), 1.00 (6H, t, J=7.5Hz);
TLC : Rf 0.46 (chloroform:methanol:water=9:1:0.1).

Example 2(276)

4-(piperazin-4-ylsulfonyll-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

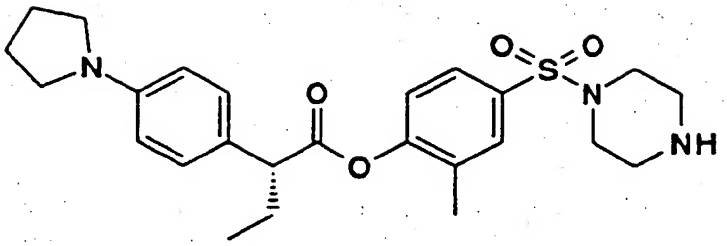


• 2HCl

NMR (CD_3OD): δ 7.71 (6H, m), 7.22 (1H, d, J=8.0Hz), 4.00 (1H, t, J=8Hz), 3.81 (4H, m), 3.31 (8H, s), 2.33 (4H, m), 2.24 (1H, m), 2.07 (3H, s), 1.98 (1H, m), 1.01 (3H, t, J=7.4Hz);
TLC : Rf 0.66 (chloroform:methanol:water=4:1:0.1).

Example 2(277)

4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2hydrochloride

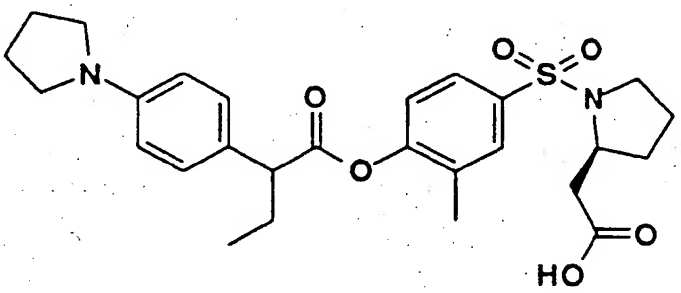


• 2HCl

NMR (CD_3OD): δ 7.70 (6H, m), 7.22 (1H, d, J=8.0Hz), 4.00 (1H, t, J=8Hz), 3.81 (4H, m), 3.30 (8H, s), 2.32 (4H, m), 2.24 (1H, m), 2.06 (3H, s), 1.99 (1H, m), 1.00 (3H, t, J=7.4Hz);
TLC : Rf 0.66 (chloroform:methanol:water=4:1:0.1).

Example 2(278)

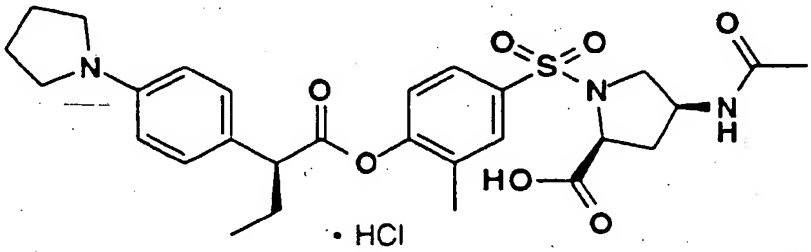
4-((2S-carboxymethylpyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



NMR ($CDCl_3$): δ 7.70-7.58 (2H, m),7.23 (2H, d, J=8Hz), 7.09 (1H, d, J=8Hz), 6.55 (2H, d, J=8Hz), 4.00-3.84 (1H, m), 3.62 (1H, t, J=7Hz), 3.50-3.35 (1H, m), 3.35-3.20 (4H, m), 3.18-3.03 (2H, m), 2.54 (1H, dd, J=15, 10Hz), 2.30-1.40 (13H, m), 0.98 (3H, t, J=7Hz);
TLC : Rf 0.39 (hexane:ethyl acetate:acetic acid=50:50:1).

Example 2(279)

4-((2S-carboxy-4-acetylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



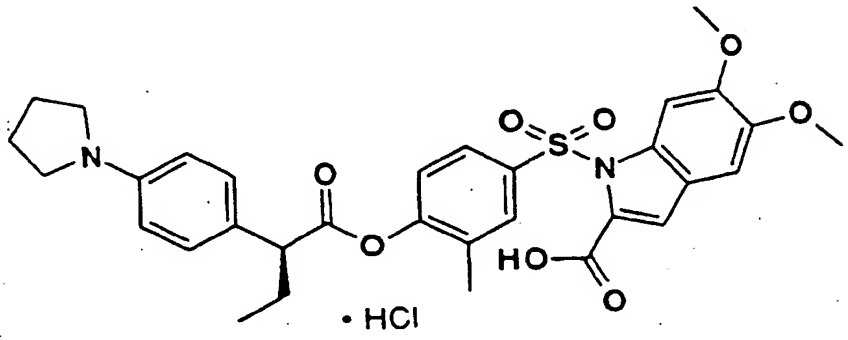
• HCl

NMR ($DMSO-d_6$): δ 8.02 (1H, d, J=6Hz), 7.74 (1H, s), 7.69 (1H, d, J=8.8Hz), 7.24 (2H, d, J=8.6Hz), 7.18 (1H, d, J=8.6Hz), 6.69 (1H, d, J=8.8Hz), 4.15 (1H, t, J=7Hz), 3.75 (2H, ml, 3.51 (1H, m), 3.28 (4H, ml, 3.05 (1H, m), 2.33 (1H, m), 2.12 (1H, m), 1.99 (7H, s-like), 1.83 (2H, m), 1.75 (3H, s), 0.91 (3H, t, J=7.4Hz);

TLC : Rf 0.67 (chloroform:methanol:water=6:4:1).

Example 2(280)

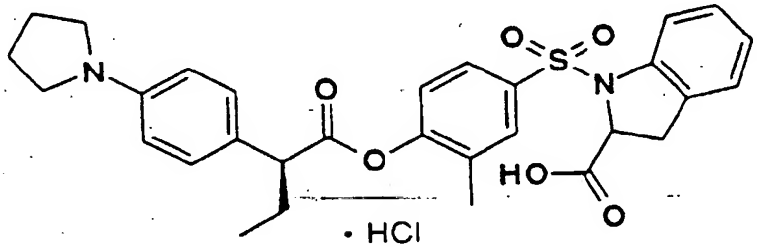
4-((2-carboxy-5,6-dimethoxyindol-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 7.87 (1H, d, J=2.2Hz), 7.79 (1H, dd, J=8.6Hz, 2.2Hz), 7.50 (1H, s), 7.25-7.13 (5H, m), 6.66 (2H, d, J=8.0Hz), 3.88 (3H, s), 3.78 (3H, s), 3.71 (1H, t, J=7.2Hz), 3.26 (4H, m), 2.08 (1H, m), 1.97 (4H, m), 1.93 (3H, s), 1.78 (1H, m), 0.88 (3H, t, J=7.6Hz);
TLC : Rf 0.45 (chloroform:methanol:water=4:1:0.1).

Example 2(281)

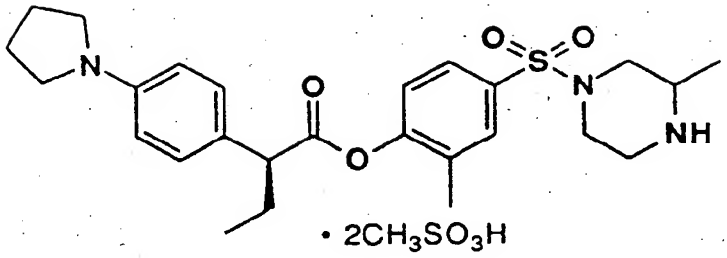
4-((2RS-carboxyindolin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (DMSO-d_6): δ 7.78 (1H, s), 7.67 (1H, dd, J=2 and 8Hz), 7.35-6.94 (7H, m), 6.80-6.64 (2H, br), 5.00-4.93 (1H, m), 3.70 (1H, t, J=7Hz), 3.39-2.96 (6H, m), 2.17-1.64 (2H, m), 2.04-1.94 (4H, m), 1.91 (3H, s), 0.87 (3H, t, J=7Hz);
TLC : Rf 0.30 (chloroform:methanol:water=4:1:0.1).

Example 2(282)

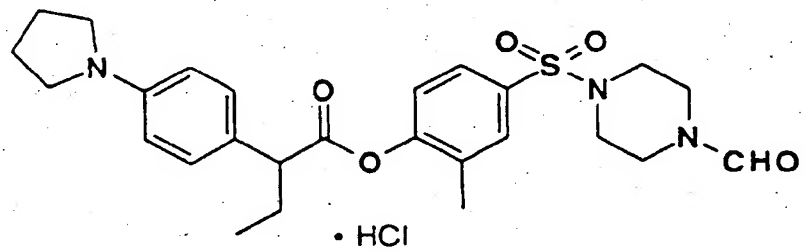
4-((2RS-methylpiperazin-4-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2methanesulfonic acid salt



NMR (CD_3OD): δ 7.75-7.60 (6H, m), 7.23 (1H, d, J=8.5Hz), 4.00 (1H, t, J=7.5Hz), 3.90-3.70 (6H, m), 3.55-3.35 (2H, m), 3.35-3.10 (1H, m), 2.80-2.65 (1H, m), 2.66 (6H, s), 2.47 (1H, t, J=10.0Hz), 2.06 (3H, s),1.31 (3H, d, J=6.5Hz), 1.00 (3H, t, J=7.5Hz);
TLC : Rf 0.45 (chloroform:methanol:water=9:1:0.1).

Example 2(283)

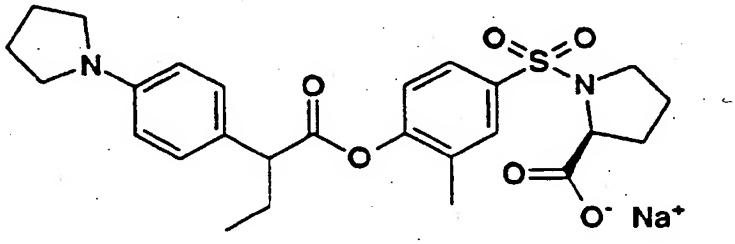
4-((4-formylpiperazin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · hydrochloride



NMR (CD_3OD): δ 7.96 (1H, s), 7.73-7.52 (6H, m), 7.19 (1H, d, J=8.4Hz), 3.97 (1H, t, J=7.6Hz), 3.88-3.67 (4H, m), 3.67-3.44 (4H, m), 3.12-2.93 (4H, m), 2.43-2.14 (5H, m), 2.12-1.81 (4H ,m), 1.00 (3H, t, J=7.2Hz);
TLC : Rf 0.38 (hexane:ethyl acetate=1:2).

Example 2(284)

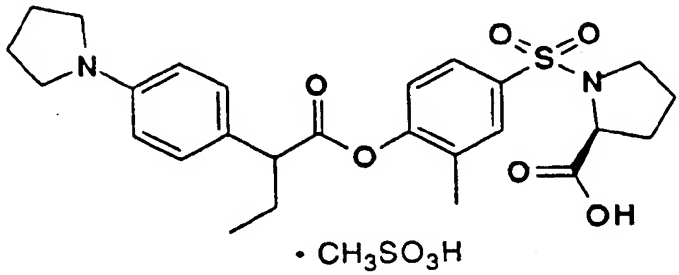
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester • sodium salt



NMR (d_6-DMSO): δ 7.78-7.64 (2H, m), 7.18 (2H, d, J=8.0Hz), 7.08 (1H, d, J=8.0Hz), 6.53 (2H, d, J=8.0Hz), 3.95-3.80 (1H, m), 3.69 (1H, t, J=7.5Hz), 3.50-3.00 (6H, m), 2.20-1.30 (10H, m), 1.96 (3H, s), 0.91 (3H, t, J=7.5Hz);
TLC : Rf 0.32 (chloroform:methanol:water=9:1:0.1).

Example 2(285)

4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · methanesulfonic acid salt

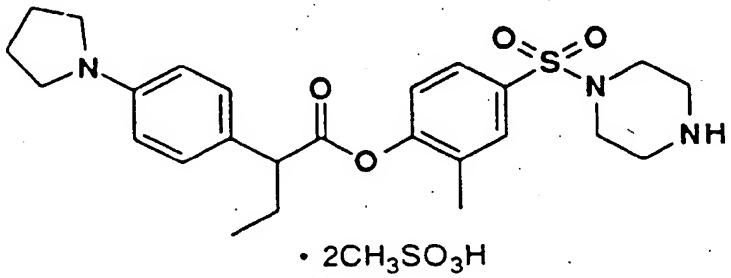


NMR ($CDCl_3$): δ 7.65 (4H, d, J=8.5Hz), 7.54 (2H, d, J=8.5Hz), 7.05 (1H, d, J=8.5Hz), 4.30-4.15 (1H, m), 4.10-3.50 (4H, m), 3.80 (1H, t, J=7.5Hz), 3.55-3.35 (1H, m), 3.30-3.10 (1H, m), 2.87 (3H, s), 2.50-1.60 (10H, m), 2.03 (3H, s), 0.99 (3H, t, J=7.5Hz);

TLC : Rf 0.32 (chloroform:methanol:water=9:1:0.1).

Example 2(286)

4-((piperazin-4-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester · 2methanesulfonic acid salt

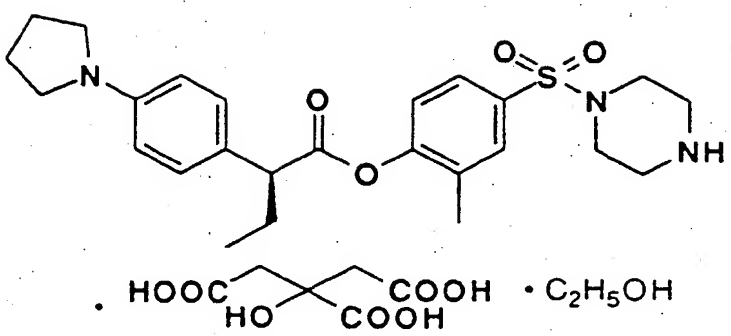


NMR (CD_3OD): δ 7.75-7.60 (6H, m), 7.23 (1H, d, J=8.0Hz), 4.01 (1H, t, J=7.5Hz), 3.90-3.70 (4H, m), 3.35-3.20 (8H, m), 2.68 (6H, s), 2.40-1.80 (6H, m), 2.06 (3H, s), 1.00 (3H, t, J=7.5Hz);

TLC : Rf 0.14 (chloroform:methanol:acetic acid=40:2:1).

Example 2(287)

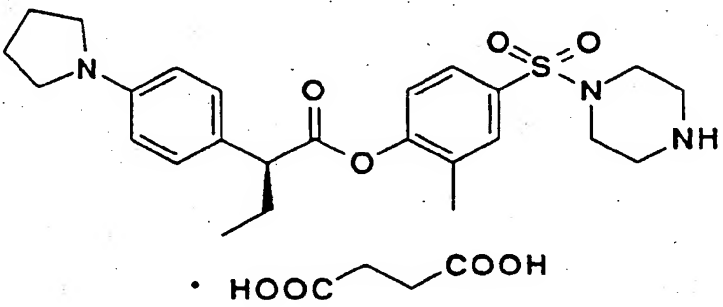
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl) butanoic acid ester · citric acid salt · ethanol salt



NMR (CD_3OD): δ 7.66 (1H, brs), 7.62 (1H, brd, J=8.0Hz), 7.20 (2H, d, J=8.5Hz), 7.18 (1H, d, J=8.0Hz), 6.58 (2H, d, J=8.5Hz), 3.67 (1H, t, J=7.5Hz), 3.60 (2H, q, J=7.0Hz), 3.40-3.15 (12H, m), 2.76 (4H, dd, J=8.0, 14.0Hz), 2.30-1.70 (9H, m), 1.17 (3H, t, J=7.0Hz), 0.97 (3H, t, J=7.5Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(288)

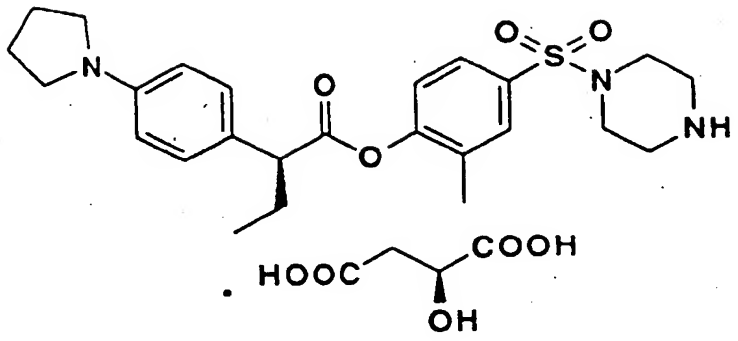
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · succinic acid salt



NMR (CD_3OD): δ 7.64 (1H, brs), 7.61 (1H, brd, J=8.0Hz), 7.19 (2H, d, J=8.5Hz), 7.17 (1H, d, J=8.0Hz), 6.57 (2H, d, J=8.5Hz), 3.64 (1H, t, J=7.5Hz), 3.40-3.20 (4H, m), 3.12 (8H, s), 2.51 (4H, s), 2.30-1.76 (9H, m), 0.97 (3H, t, J=7.5Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(289)

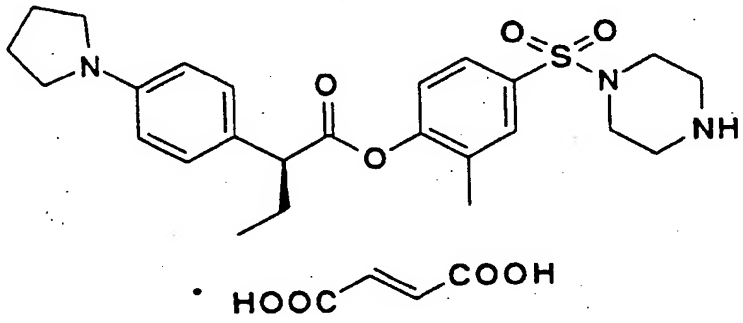
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · L-malic acid salt



NMR (CD_3OD): δ 7.67 (1H, brs), 7.62 (1H, brd, J=8.0Hz), 7.22 (2H, d, J=8.5Hz), 7.19 (1H, d, J=8.0Hz), 6.58 (2H, d, J=8.5Hz), 4.28 (1H, dd, J=5.0, 7.5Hz), 3.68 (1H, t, J=7.5Hz), 3.40-3.05 (12H, m), 2.78 (1H, dd, J=5.0, 15.0Hz), 2.52 (1H, dd, J=7.5, 15.0Hz), 2.40-1.72 (9H, m), 0.98 (3H, t, J=7.5Hz) ;
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(290)

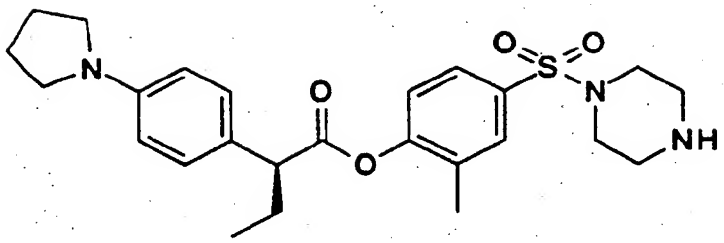
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · fumaric acid salt



NMR (CD_3OD): δ 7.68 (1H, brs), 7.63 (1H, brd, J=8.0Hz), 7.21 (2H, d, J=8.5Hz), 7.19 (1H, d, J=8.0Hz), 6.82 (2H, s), 6.59 (2H, d, J=8.5Hz), 3.65 (1H, t, J=7.5Hz), 3.40-3.10 (12H, m), 2.30-1.70 (9H, m), 0.98 (3H, t, J=7.5Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(291)

4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · oxalic acid salt

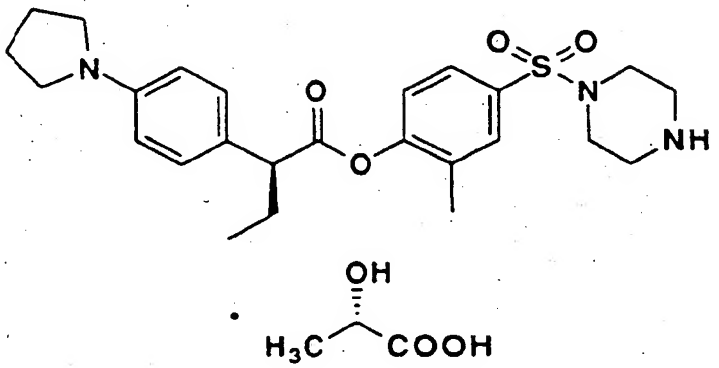


• $(COOH)_2$

NMR (CD_3OD): δ 7.68 (1H, s), 7.63 (1H, brd, J=8.0Hz), 7.20 (2H, d, J=8.5Hz), 7.19 (1H, d, J=8.0Hz), 6.60 (2H, d, J=8.5Hz), 3.66 (1H, t, J=7.5Hz), 3.45-3.10 (12H, m), 2.30-1.75 (9H, m), 0.98 (3H, t, J=7.5Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(292)

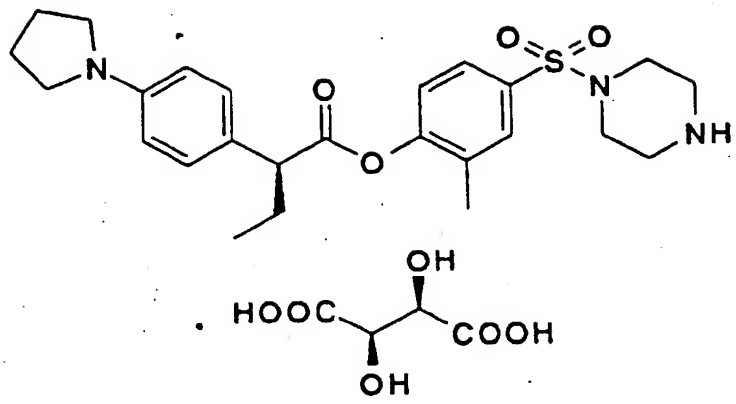
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · L-lactic acid salt



NMR (CD_3OD): δ 7.65 (1H, s), 7.61 (1H, brd, J=8.0Hz), 7.20 (2H, d, J=8.5Hz),7.17 (1H, d, J=8.0Hz), 6.57 (2H, d, J=8.5Hz), 4.04 (1H, q, J=7.0Hz), 3.65 (1H, t, J=7.5Hz), 3.40-3.20 (4H, m), 3.14 (8H, s), 2.15 (3H, s), 2.20-1.75 (6H, m), 1.31 (3H, d, J=7.0Hz), 0.97 (3H, t, J=7.5Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(293)

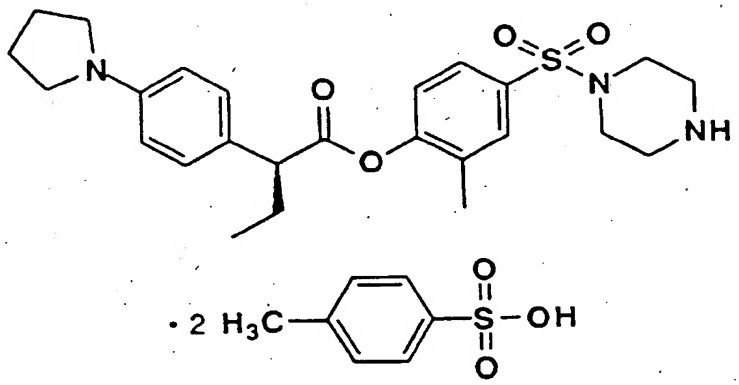
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · L-tartaric acid salt



NMR (CD_3OD): δ 7.68 (1H, s), 7.64 (1H, brd, J=8.0Hz), 7.21 (2H, d, J=8.5Hz), 7.18 (1H, d, J=8.0Hz), 6.59 (2H, d, J=8.5Hz), 4.43 (2H, s), 3.68 (1H, t, J=7.5Hz), 3.45 - 3.10 (12H, m), 2.40 - 1.78 (9H, m), 0.98 (3H, t, J=7.5Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(294)

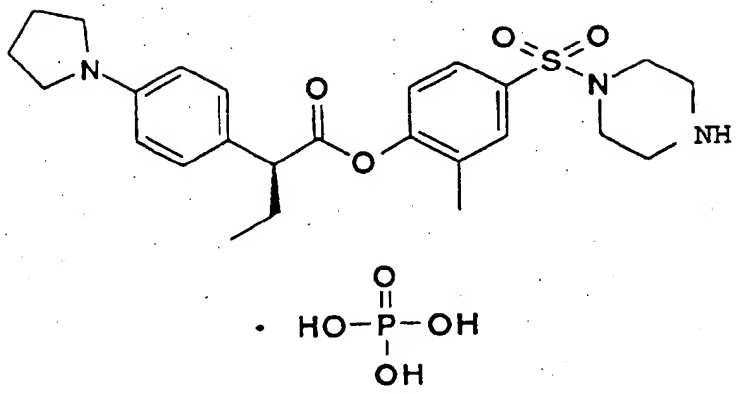
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · 2 p-toluenesulfonic acid salt



NMR (CD_3OD): δ 7.68 (6H, d, J=8.0Hz), 7.63 (4H, d, J=9.0Hz), 7.22 (5H, d, J=8.0Hz), 3.99 (1H, t, J=7.4Hz),3.83 - 3.65 (4H, m), 3.30 (8H, m), 2.36 (6H, s), 2.36-2.20 (5H, m), 2.04 (3H, s), 1.95 (1H, m), 0.99 (3H, t, J=7.4Hz);
TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(295)

4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · phosphoric acid salt

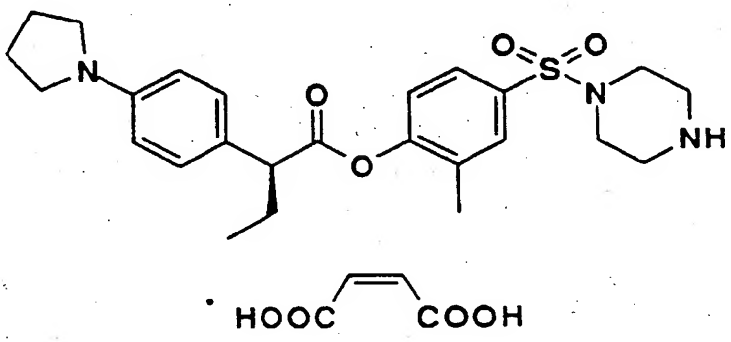


NMR (DMSO-d_6): δ 8.00-7.40 (3H, m), 7.67 (1H, brs), 7.62 (1H, brd, J=8.8Hz), 7.25 (1H, d, J=8.8Hz), 7.21 (2H, d, J=8.8Hz), 6.56 (2H, d, J=8.8Hz), 3.75 (1H, t, J=7.4Hz), 3.23 (4H, brs), 2.94 (8H, brs), 2.01 (3H, s), 2.20-1.80 (6H, m), 0.93 (3H, t, J=7.4Hz);

TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 2(296)

4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester · maleic acid salt

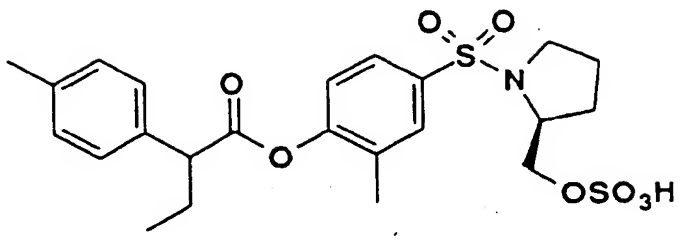


NMR (CD_3OD): δ 7.67 (1H, s), 7.62 (1H, brd, J=8.0Hz), 7.20 (2H, d, J=8.5Hz), 7.19 (1H, d, J=8.0Hz), 6.58 (2H, d, J=8.5Hz), 6.23 (2H, s), 3.65 (1H, t, J=7.5Hz), 3.40-3.05 (12H, m), 2.30-1.78 (6H, m), 1.98 (3H, s), 0.97 (3H, t, J=7.5Hz);

TLC : Rf 0.11 (chloroform:methanol:acetic acid=40:2:1).

Example 3

4-(2S-hydroxysulfonyloxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester



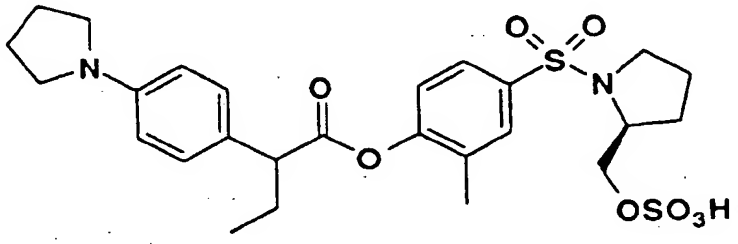
To a solution of the compound prepared in example 2(19) (690 mg) in pyridine (10 ml) was added sulfur trioxide pyridine complex (766 mg) and the reaction mixture was stirred for 30 min at room temperature. The reaction mixture was concentrated, and the residue was purified by column chromatography on silica gel (chloroform:methanol=10:1) to give the title compound (700 mg) having the following physical data.

NMR (DMSO-d_6): δ 7.74 (1H, d, J=2.0Hz), 7.67 (1H, dd, J=8.5, 2.0Hz), 7.30 (2H, d, J=8.5Hz), 7.20 (2H, d, J=8.5Hz), 7.18 (1H, d, J=8.5Hz), 3.94-3.78 (2H, m), 3.76-3.60 (1H, m), 3.58 (1H, t, J=7.0Hz), 3.3-3.2 (1H, m), 3.12-2.94 (1H, m), 2.31 (3H, s), 2.25-2.00 and 1.95-1.70 (each 1H, m), 1.97 (3H, s), 1.90-1.60 (2H, m), 1.60-1.30 (2H, m), 0.91 (3H, t, J=7.5Hz);

TLC : Rf 0.39 (water:methanol:chloroform=1:10:40).

Example 3(1)

4-(2S-hydroxysulfonyloxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester



By the same procedure as example 3, the title compound having the following physical data was given by using the compound prepared in example 2(10).

NMR (DMSO-d_6): δ 7.74 (1H, s), 7.67 (1H, d, J=8.5Hz), 7.25-7.10 (3H, m), 6.55 (2H, d, J=8.0Hz), 3.91 (1H, d, J=8.5Hz), 3.80-3.50 (3H, m), 3.40-3.20 (1H, m), 3.35-3.20 (4H, m), 3.15-2.90 (1H, m), 2.20-1.60 (2H, m),1.98 (3H, s), 2.05-1.90 (4H,m), 1.90-1.60 (2H,m), 1.60-1.30 (2H,m), 0.91 (3H,t,J=7.5Hz);

TLC:Rf 0.38 (water:methanol:chloroform=1:10:40).

Formulation Examples

Formulation Example 1

The following components were admixed in conventional manner and punched out to obtain 100 tablets each containing 50 mg of active ingredient.

4-(piperazin-4-yl sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester 2 hydrochloride	5.0g
Carboxymethylcellulose calcium (disintegrating agent)	0.2g
Magnesium stearate (lubricating agent)	0.1g
Microcrystalline cellulose	4.7g

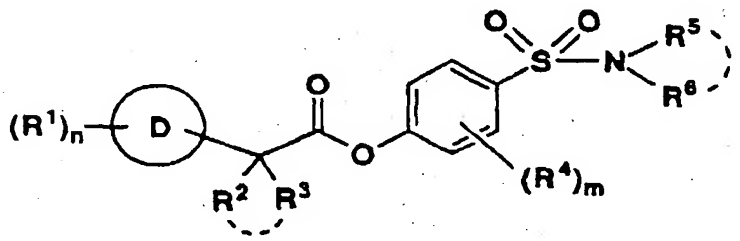
Formulation Example 2

The following components were admixed in conventional manner. The solution was sterilized in conventional manner, placed 5 ml portion into ampoules and freeze-dried to obtain 100 ampoules each containing 20 mg of the active ingredient.

4-(piperazin-4-yl sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester 2 hydrochloride	2.0g
mannitol	20 g
Distilled water	1000ml

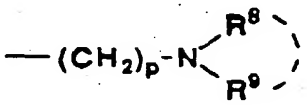
Claims

1. A sulfonamide derivative of the formula (I)

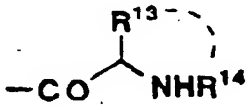


(I)

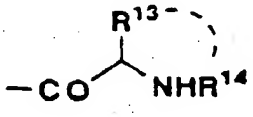
wherein R^1 is C1-8 alkyl, C1-8 alkoxy, hydroxy, keto, nitro, halogen atom, trihalomethyl, cyano, amidino, $-COOR^7$ (in which R^7 is hydrogen atom or C1-8 alkyl), or



(in which p is an integer from 0 to 4, and
R^8 and R^9 each, independently, is hydrogen atom, C1-4 alkyl, C2-5 acyl, $-COOR^{10}$ (in which R^{10} is hydrogen atom or C1-8 alkyl), $-CONR^{11}R^{12}$ (in which R^{11} and R^{12} each, independently, is hydrogen atom or C1-4 alkyl),

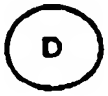


(in which

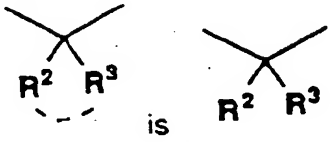


Is an α-amino acid residue), or
R^8 and R^9 taken together with the nitrogen atom to which they are attached represent an aliphatic heterocyclic

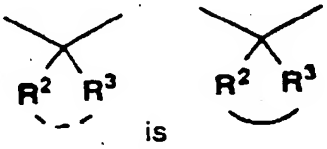
ring which is unsubstituted or substituted by C1-4 alkyl or phenyl C1-4 alkyl);
n is an integer from 0 to 5;



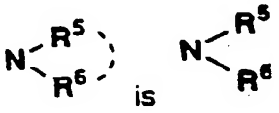
is a carbocyclic ring or heterocyclic ring;



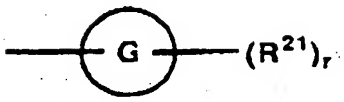
in which R^2 and R^3 each, independently, is hydrogen atom, C1-4 alkyl, C1-4 alkoxy, halogen atom, trihalomethyl or phenyl, or
R^2 and R^3, taken together, represent C1-4 alkylidene, or



in which R^2 and R^3, taken together with the carbon atom to which they are attached represent C3-7 cycloalkyl;
R^4 is C1-4 alkyl or C1-4 alkoxy or two of R^4, attached to the benzene nucleus at ortho positions relative to each other, taken together, represent C3-5 alkylene;
m is an integer from 0 to 4; and

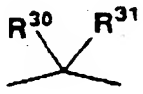


in which R^5 and R^6 each, independently, is
1) hydrogen atom,
2) hydroxy,
3) C1-8 alkyl,
4) C1-8 alkoxy
5) phenyl C1-4 alkoxy,
6) amidino,
7) -M-R^{16}
(in which M is single bond or C1-8 alkylene), and
R^{16} is
i) -$NR^{17}R^{18}$ (in which R^{17} and R^{18} each, independently, is hydrogen atom or C1-4 alkyl),
ii) -$CONR^{19}R^{20}$ (in which R^{19} and R^{20} each, independently, is hydrogen atom or C1-4 alkyl),
iii)

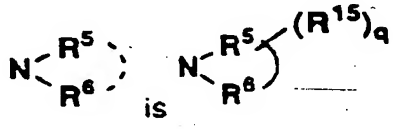


(in which

is a carbocyclic ring,
r is an integer from 0 to 5, and
R^{21} is C1-4 alkyl, C1-4 alkoxy, nitro, amidino, -$COOR^{22}$ (in which R^{22} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl), -SO_3H, -$CONR^{23}$-E-R^{24} (in which R^{23} is hydrogen atom or C1-4 alkyl, E is 1-4 alkylene and R^{24} is -$COOR^{25}$ (in which R^{25} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl) or tetrazole ring), tetrazole ring or morpholino ring),
iv) heterocyclic ring, unsubstituted or substituted by 1 to 4 substituents selected from C1-4 alkyl, C1-4 alkoxy, hydroxy, phenyl C1-4 alkyl, -$COOR^{28}$ (in wich R^{26} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl), hydroxy C1-4 alkyl or C2-4 alkoxyalkyl),
8) C1-8 alkyl substituted by one or two of -OR^{27} (in which R^{27} is hydrogen atom, C1-4 alkyl, C2-4 alkoxyalkyl or C2-4 alkyl substituted by -OR^{28} (in which R^{28} is hydrogen atom or C2-4 alkoxyalkyl)),
9) -J-$COOR^{29}$ (in which R^{29} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl, and
J is a single bond, -$(CH_2)_s$- or



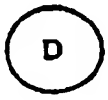
(in which s is an integer from 2 to 6, and
R^{30} and R^{31} each, independently, is
i) hydrogen atom,
ii) C1-8 alkyl,
iii) -$COOR^{32}$ (in which R^{32} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl),
iv) carbocyclic or heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, amino, nitro, hydroxy, halogen atom, nitrite, guanidino and amidino, or
v) C1-8 alkyl substituted by one or more substituents selected from hydroxy, -$COOR^{33}$ (in which R^{33} is hydrogen atom, C1-8 alkyl, phenyl or phenyl C1-4 alkyl), -$NR^{34}R^{35}$ (in which R^{34} and R^{35} each, independently, is hydrogen atom or C1-4 alkyl), carbocyclic or heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, amino, nitro, hydroxy, halogen atom, nitrile, guanidino and amidino, with the proviso that a carbon atom of C1-8 alkyl may be replaced by a sulfur atom), or



in which R^5 and R^6, taken together with the nitrogen atom to which they are attached represent a heterocyclic ring,
q is an integer from 0 to 4, and
R^{15} is
1) hydroxy,

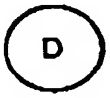
2) keto,
3) protected keto,
4) C1-4 alkyl,
5) C1-4 alkoxy,
6) phenyl,
7) phenoxy,
8) phenyl C1-4 alkyl,
9) phenyl C1-4 alkoxy,
10) nitro,
11) -$COOR^{36}$ (in which R^{36} is hydrogen atom, C1-8 alkyl, C1-4 alkyl substituted by -$CONR^{37}R^{38}$ (in which R^{37} and R^{38} each, independently, is hydrogen atom or C1-4 alkyl), C1-4 alkyl substituted by -$NR^{39}R^{40}$ (in which R^{39} and R^{40} each, independently, is hydrogen atom or C1-4 alkyl), C1-4 alkyl substituted by -OR^{41} (in which R^{41} is C2-4 alkyl substituted by -OR^{42} (in which R^{42} is hydrogen atom or C2-4 alkoxyalkyl)) or C1-4 alkyl substituted by piperazino ring),
12) -$NR^{43}R^{44}$ (in which R^{43} and R^{44} each, independently, is hydrogen atom, C1-4 alkyl or C2-5 acyl),
13) -$CONR^{45}R^{46}$ (in which R^{45} and R^{46} each, independently, is hydrogen atom, hydroxy, C1-4 alkyl, phenyl C1-4 alkyloxy or C1-4 alkyl substituted by hydroxy or -$COOR^{47}$ (in which R^{47} is hydrogen atom or C1-8 alkyl),),
14) C1-4 alkyl substituted by one or more substituents selected from hydroxy, -$COOR^{48}$ (in which R^{48} is hydrogen atom or C1-8 alkyl), -$NR^{49}R^{50}$ (in which R^{49} and R^{50} each, independently, is hydrogen atom or C1-4 alkyl), -OSO_3H or 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,
15) 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,
16) halogen atom,
17) -CHO, or
18) -NR^{51}-$COOR^{52}$ (in which R^{51} and R^{52} each, independently, is hydrogen atom or C1-8 alkyl);
or a non-toxic salt, acid addition salt or solvate thereof.

2. A compound according to claim 1, wherein



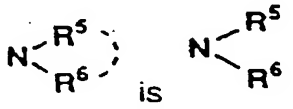
is 3-15 membered mono- or poly-cyclic aromatic hydrocarbon ring or aliphatic hydrocarbon ring.

3. A compound according to claim 1, wherein



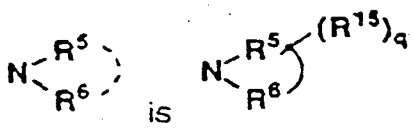
is 5-15 membered mono- or bi-cyclic aromatic heterocyclic ring, saturated heterocyclic ring or partly saturated heterocyclic ring containing one to four nitrogen atoms, one or two sulfur atoms, one or two oxygen atoms or one nitrogen atom and one sulfur atom or oxygen atom.

4. A compound according to any one of claims 1 to 3, wherein



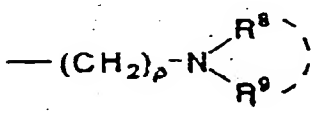
in which all symbols are as defined in claim 1.

5. A compound according to any one of claims 1 to 3, wherein

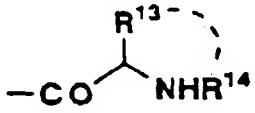


in which all symbols are as defined in claim 1.

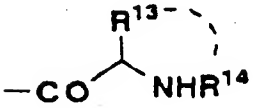
6. A compound according to any one of claims 1 to 5, wherein R^1 is C1-8 alkyl, C1-8 alkoxy, hydroxy, keto, nitro, halogen atom, trihalomethyl, cyano, amidino, -COOR^7 (in which R^7 is as defined in claim 1), or



(in which p is as defined in claim 1, and
R^8 and R^9 each, independently, is hydrogen atom, C1-4 alkyl, C2-5 acyl, -COOR10 (in which R^{10} is as defined in claim 1), -CONR^{11}R^{12} (in which R^{11} and R^{12} are as defined in claim 1),

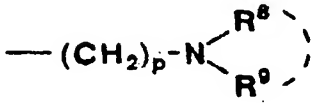


(in which



is as defined in claim 1).

7. A compound according to any one of claims 1 to 5, wherein R^1 is



in which R^8 and R^9 taken together with the nitrogen atom to which they are attached represent an aliphatic heterocyclic ring which is unsubstituted or substituted by C1-4 alkyl or phenyl C1-4 alkyl.

8. A compound according to claim 1, which is

4-(2S-t-butyloxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid

ester,
4-(2S-hydroxymethylpyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-oxopyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester,
4-(pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl) phenyl)butanoic acid ester,
4-(2S-(pyrrolidin-1-ylmethyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(pyrrolidin-1-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester,
4-(indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(ethoxycarbonyl)indolin-1-ylsulfonyl)2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(ethoxycarbonyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(N,N-dimethylaminocarbonylmethoxycarbonyl)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(N-benzyloxycarbamoyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(6-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(6-aminoindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(7-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(7-aminoindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(benzimidazol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(morpholin-4-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(6-aza-7-oxo-bicyclo[3.2.1]octan-6-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-benzylpiperazin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-(2-hydroxyethyl)piperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-hydroxymethylpiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-(N,N-dimethylamino)piperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-(pyrimidin-2-yl)piperazin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(1,4-dioxa-8-azaspiro[4.5]decan-8-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(3-azabicyclo[3.2.2]nonan-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]octan-6-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-oxopiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-oxo-4S-benzyltetrahydroxazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-oxo-4S-isopropylperhydroxazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-oxo-4S-methyl-5S-phenylperhydroxazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(1RS-oxo-4S-methoxycarbonylperhydrothiazol-3-ylsulsonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(morpholin-4-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(imidazol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(morpholin-4-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(morpholin-4-ylsulfonyl)phenyl 1-(4-nitrophenyl) cyclobutanecarboxylic acid ester,
4-(6-aza-7-oxobicyclo[3.2.1]octan-6-ylsulfonyl)phenyl 2-,4-methoxyphenyl)-2-ethylbutanoic acid ester,
4-(morpholin-4-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(imidazol-1-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester,
4-(morpholin-4-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phen 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-1RS-(ethoxycarbonyl)-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-phenyl-2-methoxyacetic acid ester,
4-(N-benzyloxycarbonylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1RS-phenyl-2RS-methylbutylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-sulfamoylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-methoxyethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-methoxyethyl-N-benzylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-t-butyloxysulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,

4-(N-4-hydroxybutylsultamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1RS-hydroxymethyl-2-methylpropylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2RS,3-dihydroxypropylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-benzyloxysulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(N',N'-dimethylamino)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(N'-methylamino)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(carbamoylmethyl)sulfamoyl)phenyl 2RS-(4-(pyrrolidln-1-yl)phenyl)butanoic acid ester,
4-(N-t-butylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-adamantan-1-ylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-guanidinosulfonyl-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2RS,3-dihydroxypropylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N,N-bis(2-(methoxymethoxy)ethyl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N,N-bis(2-(2-(methoxymethoxy)ethoxy)ethyl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl) butanoic acid ester,
4-(N-methyl-N-methoxysulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-benzylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N',N'-dimethylamino)ethylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-guanidinosulfonylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-guanidinosulfonylphenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-2RS,3-dihydroxypropylsulfamoyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(N-2-methoxyethylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N',N'-dimethylamino)ethylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester,
4-(guanidinosulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(N,N-diethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-benzylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-methyl-N-benzylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-2-phenylethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-methyl-N-2-phenylethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-1RS-(4-methylphenyl)butylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-2-(pyridin-2-yl)ethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(piperidin-1-yl)ethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(tetrazol-5-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(morpholin-4-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanolc acid ester,
4-(N-(pyrrolidin-3-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(1-benzylpipelidin-4-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(pyridin-2-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(pyrazin-2-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(imidazol-2-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(quinuclidin-3RS-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(2,2,6,6-tetramethylpiperidin-4-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(quinuclidin-3RS-yl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(morpholin-4-yl)ethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(piperazin-4-yl)ethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(piperidin-4-yl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(morpholin-4-yl)ethylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-2-(pyridin-2-yl)ethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(piperidin-1-yl)ethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(1-methylpyrrol-2-yl)ethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-(tetrazol-5-ylmethyl)sulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-(tetrazol-5-ylmethyl)sulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-(tetrazol-5-yl)sulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-(tetrazol-5-yl)sulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-(quinuclidin-3RS-yl)sulfamoyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(N-2R-methoxy-3R-hydroxy-4S-hydroxy-5R-hydroxyperhydropyran-6R-ylmethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-phenylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,

4-(N-4-nitrophenylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-phenylsulfamoyl)phenyl 2RS-(4-aminophenyl)butanoic acid ester,
4-(N-(2-(tetrazol-5-yl)phenyl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-4-(morpholin-4-yl)phenylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
2-(N-(4-(2RS-(4-(pyrrolidin-1-yl)phenyl)butylyloxy)-3-methylphenyl sulfonyl)amino)phenylsulfonic acid
4-(N-3,5-dimethoxyphenylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-phenylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-(tetrazol-5-ylmethyl)carbamoyl)benzen-1-ylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-2-(N'-(tetrazol-5-ylmethyl)carbamoyl)benzen-1-ylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-(4-amidinophenyl)sulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-(4-amidinophenyl)sulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(tetrazol-5-yl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-4-(morpholin-4-yl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(tetrazol-5-yl)phenylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-t-butyloxycarbonylamino)phenyl)butanoic acid ester,
4-(3,5-dimethoxybenzylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((4-t-butoxycarbonylaminopiperidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-methoxy-N-benzylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-benzyloxy-N-methylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(N,N-dimethylamino)ethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(piperidin-1-yl)ethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(3-(morpholin-4-yl)propylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2-oxo-4R-isopropylperhydroxazol-3-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(morpholin-4-yl)ethyl-N-methoxyaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(5-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(morpholin-4-ylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(6-fluoroindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(5-(N,N-dimethylamino)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-methylpiperazin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(5-nitroindolin-1-ylsulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-ethylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-ethylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-methyl-1,4-perhydrodiazepin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-ethoxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2S -(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(quinuclidin-3RS-ylaminosulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-(morpholin-4-yl)ethylaminosulfonyl)-2-methylphenyl 2RS-4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(3,5-dimethoxyphenylaminosulfonyl)-2-methylphenyl 2RS-4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2R-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxy-4R-hydroxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxy-4R-benzyloxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxy-4S-aminopyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxy-4R-aminopyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-(N-carboxymethylcarbamoyl)pyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,

4-(2S-(2-aminoethoxycarbonyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-(2-(2-hydroxyethoxy)ethoxycarbonyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-hydroxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-(2-(piperazin-4-yl)ethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2-(2-methoxyphenyl)-2-ethylbutanoic acid ester,
4-(2S carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(2-methoxyphenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2S-(2-(piperazin-1-yl)ethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2S-(2-(2-hydroxyethoxy)ethoxycarbonyl)pyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2S-(2-aminoethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2S-hydroxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2S-(2-aminoethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2S-(2-(piperazin-4-yl)ethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2S-(2-(2-hydroxyethoxy)ethyl)oxycarbonylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2R-(4-nitrophenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2S-(4-nitrophenyl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(2R-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(2H-carboxypyrrolidin-1-ylsulfonyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-phenylbutanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-carboxyindol-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-carboxyperhydroindol-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(N-carboxymethylcarbamoyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-carboxy-3,3-dimethylindolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methoxyphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(N-2-carboxyethylcarbamoyl)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(N-2-hydroxyethylcarbamoyl)indolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-carboxy-5,6-dimethoxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(2-aminoethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-carboxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-yl)phenyl)butanoic acid ester,
4-(2RS-carboxy-5,6-dimethoxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2-carboxy-5-hydroxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(2-(2-hydroxyethoxy)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-hydroxymethylindolin-1-ylsulfonyl)-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,

4-(2RS-carboxy-5-hydroxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(2-(piperazin-1-yl)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-(N-hydroxycarbamoyl)indolin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2-carboxy-5,6-dimethoxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2-carboxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2-carboxy-5-hydroxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2RS-hydroxymethylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2RS-(2-aminoethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2RS-(2-(piperazin-4-yl)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-melhoxyphenyl)butanoic acid ester,
4-(2RS-(2-(2-hydroxyethoxy)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(3-methoxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(2-methoxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(2-methoxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(3,4-dimethoxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(3,4-dimethoxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2-carboxy-5,6-dimethoxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2-carboxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2-carboxy-5-hydroxyindol-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2RS-(2-aminoethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2RS-hydroxymethylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2RS-(2-(2-hydroxyethoxy)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2RS-(2-(piperazin-4-yl)ethyl)oxycarbonylindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-hydroxyphenyl)butanoic acid ester,
4-(2RS-carboxyindolin-1-ylsulfonyl)phenyl 2RS-(4-aminophenyl)butanoic acid ester,
4-(4S-carboxyperhydrothiazol-3-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-carboxypiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-carboxypiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(3RS-carboxypiperidin-1-ylsulfonyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4S-carboxyperhydrothiazol-3-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2RS-carboxymorpholin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(1S-oxo-4S-carboxyperhydrothiazol-3-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4S-carboxy-1,1-dioxoperhydrothiazol-3-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-(2-hydroxyethyl)piperazin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4-carboxymethylpiperazin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(4S-carboxyperhydrothiazol-3-ylsulfonyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-carboxymethyl-N-2-methoxyethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1RS,2-dicarboxyethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(1-carboxycyclobutane)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1RS-carboxy-2-phenylethylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1S-carboxy-2-methylpropylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(1S-carboxy-2-carboxymethylthioethyl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,

4-(N-1RS-carboxy-1-(thiophen-2-yl)methylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1RS-carboxy-1-(furan-2-yl)methylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-carboxymethyl-N-2-methoxyethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-propyl-N-carboxymethylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-1S-carboxy-5-aminopentylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-carboxymethylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester,
4-(N-2-methoxyethyl-N-carboxymethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-1RS,2-dicarboxyethylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-propyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-benlyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-2-phenylethyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-phenyl-N-carboxymethylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N,N-bis(2-hydroxyethyl)sulfamoyl)-2-methyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N,N-bis(2-(2-hydroxyethoxy)ethyl)sulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(3RS-carboxy-1,4-benzodioxan-5-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2RS-hydroxy-4R-hydroxy-5R-hydroxy-6R-hydroxymethylperhydropyran-3R-ylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-3-carboxyadamantan-1-ylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(1S,4R,3R-carboxybicyclo[2.2.1]heptan-2S-yl)sulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-3S-carboxycyclohexane-1R-ylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2RS-carboxycyclohexane-1RS-ylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(naphthalen-1-yl)acetic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(naphthalen-2-yl)acetic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(cyclohexane-1-yl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-phenylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-phenyl-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-phenylpropanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2R-phenylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2S-phenylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-phenyl-2-methylpropanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclohexanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclopropanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclopentanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-phenylcyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-phenylacetic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-chloro-2-phenylacetic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-chloro-2-phenylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2,2-diphenylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-methyl-2-phenylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2R-trifluoromethyl-2-phenyl-2-methoxyacetic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2S-trifluoromethyl-2-phenyl-2-methoxyacetic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methoxyphenyl)-3-methylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-methylpropanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methoxyphenyl)propanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-methoxyphenyl)-2-ethylbutanoic acid ester,

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1(4-methoxyphenyl)cyclohexanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methoxyphenyl)cyclopentanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methoxyphenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methoxyphenyl)cyclopropanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(3,4-dimethoxyphenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3,4-dimethoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(3-methoxyphenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-methoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(2-methoxyphenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-methoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(2-methoxyphenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,6-dimethylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsultamoyl)-2-isopropylphenyl 2RS-(4-methoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(2-methylpropyloxy)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-isopropyloxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-propyloxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methylphenyl)pentanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-methylphenyl)cyclopentanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(3-methylphenyl)cyclopentanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-methylphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(2-methylphenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-nitrophenyl)-2-methylpropanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclopropanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclopentanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-nitrophenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-methylphenyl 2RS-(4-nitrophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-methylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-3-methylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dimethylphenyl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
7-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dihydroinden-4-yl 1-(4-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-3-methylphenyl 2RS-(4-(pyrrolidin-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dimethylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-(pyrrolidin-1-yl)phenyl)cyclobutanecarboxylic acid ester,
7-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,3-dihydroinden-4-yl 2RS-(4-(pyrrolidin-1-yl)phenyl) butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2,6-dimethylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)-2-isopropylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(piperidin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(perhydroazepin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(4-aminophenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-aminophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N,N-dimethylamino)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-(N,N-dimethylamino)phenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N,N-diethylaminomethyl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymothylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-hydroxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-cyanophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-carboxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-trifluoromethylphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-amidinophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(imidazolin-2-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-chlorophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-chlorophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(2-chlorophenyl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(2-chlorophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-chlorophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-hydroxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-chloro-5-nitrophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(2-chloro-5-nitrophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(3-nitro-4-chlorophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-chlorophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-ureidophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 1-(4-ureidophenyl)cyclobutanecarboxylic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-(2S-aminopropionyl)amino)phenyl) butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-(2S-amino-3-methylbutylyl)amino) phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-(pyrrolidin-2S-ylcarbonyl)amino) phenyl)butanoic acid ester,

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3,4,5-trimethoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2,4,6-trimethylphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-methoxyphenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(3-nitro-4-aminophenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-acetylamino)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(N-methyl-N-acetylamino)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(morpholin-4-ylmethyl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(4-benzylpiperazin-1-yl)phenyl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(4-(pyrrolidin-1-ylmethyl)phenyl)butanoic acid ester,
4-((1R-oxo-4S-carboxyperhydrothiazol-3-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2R-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2R-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-aminomethylpyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((4-aminopiperidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxyazetidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2RS-carboxypiperidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2-oxo-5S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(3-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4R-methoxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2R-carboxy-4R-methoxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(2-methyl-4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4R-hydroxypyrrolidin-1yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-methoxy-N-carboxymethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(2-methoxy-4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxyaziridin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N,N-bis(2-aminoethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)bulanoic acid ester,
4-(N-carboxymethyl-N-(2-(N',N'-dimethylamino)ethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-ethylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-carboxymethyl-N-bentyloxyaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(4-carboxybutyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(1,1-dimethyl-1-carboxymethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-methyl-N-hydroxyaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidln-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(2-methyl-4-nitrophenyl)butanoic acid ester,
4-(N-carboxymethylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-(1,1-dimethyl-1-carboxymethyl)-N-propylaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,

4-((2S-carboxy-4S-aminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4R-aminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-carboxymethyl-N-(2-(morpholin-4-yl)ethyl)aminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4S-acetylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)-2-butenic acid ester,
4-((2S-carboxy-4R-acetylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2RS-carboxy-5-nitroindolin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(2-methoxy-4-nitrophenyl)butanoic acid ester,
4-((2S-carboxy-4S-methylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4S-(N,N-dimethylamino)pyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(N-hydroxyaminosulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S,6S-dimethylpiperazin-4-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2RS-methylpiperazin-4-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4R-(N,N-dimethylamino)pyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4R-methylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(piperazin-4-ylsulfonyl)-2-ethylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(piperazin-4-ylsulfonyl)-2-ethylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(piperazin-4-ylsulfonyl)-2-methylphenyl 2R-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxymethylpyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxy-4-acetylaminopyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2-carboxy-5,6-dimethoxyindol-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2RS-carboxyindolin-1-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2RS-methylpiperazin-4-yl)sulfonyl)-2-methylphenyl 2S-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((4-formylpiperazin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-((2S-carboxypyrrolidin-1-yl)sulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,
4-(2S-hydroxysulfonyloxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-methylphenyl)butanoic acid ester,
4-(2S-hydroxysulfonyloxymethylpyrrolidin-1-ylsulfonyl)-2-methylphenyl 2RS-(4-(pyrrolidin-1-yl)phenyl)butanoic acid ester,

or a non-toxic salt, acid addition salt or solvate thereof.

9. A compound according to claim 1, which is

4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(2H-1,4-benzoxazin-3-on-6-yl)butanoic acid ester,
4-(2R-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(2H-1,4-benzoxazin-3-on-6-yl)butanoic acid ester,
4-(2S-carboxypyrrolidin-1-ylsulfonyl)phenyl 2RS-(2-methylbenzimidazol-5-yl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(1,3-benzodioxol-5-yl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(thiophen-2-yl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(1,3-benzodioxol-5-yl)-2-ethylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(thiophen-2-yl)-3-methylbutanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(pyridin-3-yl)butanoic acid ester,

4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2H-1,4-benzoxazin-3-on-6yl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-(N-methoxycarbonylamino)thiazol-4-yl) butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(2-methylbenzimidazol-5-yl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2RS-(1H-1-methyl-2-pyridon-3-yl)butanoic acid ester,
4-(N-2-(N'-carboxymethylcarbamoyl)phenylsulfamoyl)phenyl 2-(thiophen-2-yl)-2-ethylbulanoic acid ester,

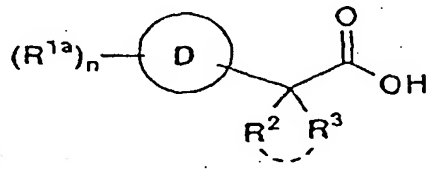
or a non-toxic salt, acid addition salt or solvate thereof.

10. A pharmaceutical composition which comprises, as active ingredient, an effective amount of a compound of the formula (I) defined in claim 1, a non-toxic salt thereof, an acid addition salt thereof or a solvate thereof, with a carrier or coating.

11. A compound of the formula (I) or a non-toxic salt thereof or a non-toxic acid addition salt thereof or solvate thereof for use in the manufacture of phamaceutical composition as an inhibitor of elastase.

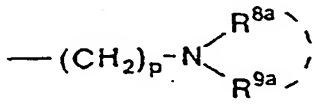
12. A compound of the formula (I) or a non-toxic salt thereof or a non-toxic acid addition salt thereof or solvate thereof for use in the manufacture of a pharmaceutical composition for the prevention and/or the treatment of diseases induced by an abnormal enhancement of the degradation of elastin, collagen fiber and/or proteoglycan, resulting from the action of elastase on a mammalian animal, especially a human (e.g., chronic obstructive pulmonary disease such as emphysema, rheumatoid arthritis, atherosclerosis, adult respiratory distress syndrome (ARDS), glomerular nephritis, myocardial infarction, idiopathic ulcerative colitis or gingivitis).

13. A process for the preparation of a sulfonamide derivative of formula (I) as defined in claim 1 which process comprises esterifying a compound of the formula:

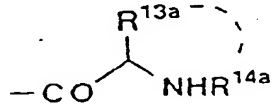


(II)

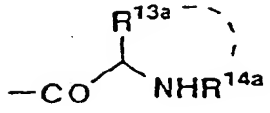
wherein R^{1a} is C1-8 alkyl, C1-8 alkoxy, hydroxy, protected hydroxy, keto, nitro, halogen atom, trihalomethyl, cyano, amidino, $-COOR^{7a}$ (in which R^{7a} is C1-8 alkyl or benzyl), or



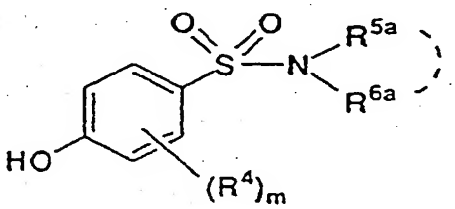
(in which p is as defined in claim 1, R^{8a} and R^{9a} each, independently, is hydrogen atom (with the proviso that, R^{8a} and R^{9a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl, C1-4 alkyl, C2-5 acyl, $-COOR^{10a}$ (in which R^{10a} is C1-8 alkyl or benzyl), $-CONR^{11}R^{12}$ (in which R^{11} and R^{12} are as defined in claim 1), or



(in which

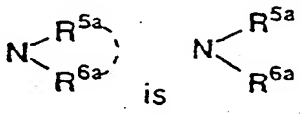


is a protected α-amino acid residue), or
R^{8a} and R^{9a}, taken together with the nitrogen atom to which they are attached represent an aliphatic heterocyclic ring which is unsubstituted or substituted by C1-4 alkyl or phenyl C1-4 alkyl, and the other symbols are as defined in claim 1 with a compound of formula (III)

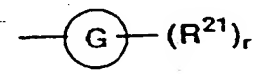


(III)

wherein

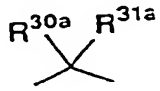


(in which R^{5a} and R^{6a} each, independently, is
1) hydrogen atom (with the proviso that, R^{5a} and R^{6a} do not represent hydrogen atom at the same time),
2) hydroxy,
3) hydroxy protected by a protecting group which is removable under acid conditions,
4) t-butoxycarbonyl,
5) benzyloxycarbonyl,
6) C1-8 alkyl,
7) C1-8 alkoxy,
8) phenyl C1-4 alkoxy,
9) amidino,
10) -M-R^{16a} (in which M is as defined in claim 1, and R^{16a} is i) -$NR^{17a}R^{18a}$ (in which R^{17a} and R^{18a} each, independently, is hydrogen atom (with the proviso that, R^{17a} and R^{18a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), ii) -$CONR^{19}R^{20}$ (in which R^{19} and R^{20} are as defined in claim 1),

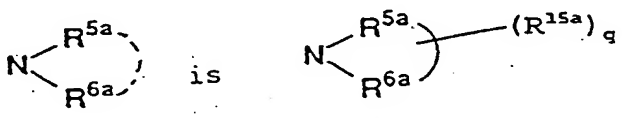
iii) 

(in which all the symbols are as hereinbefore defined), iv) heterocyclic ring, unsubstituted or substituted by 1 to 4 substituents selected from C1-4 alkyl, C1-4 alkoxy, hydroxy, phenyl C1-4 alkyl, -$COOR^{26}$ (in which R^{26} is as defined in claim 1), hydroxy C1-4 alkyl in which hydroxy is protected by a protecting group which is removable under acid conditions or C2-4 alkoxyalkyl),
11) C1-8 alkyl substituted by one or two of -OR^{27a} (in which R^{27a} is hydrogen atom, C1-4 alkyl, C2-4 alkoxyalkyl, t-butyldimethylsilyl, THP, benzyl, or C2-4 alkyl substituted by -OR^{28a} (in which R^{28a} is hydrogen atom, C2-4 alkoxyalkyl, t-butyldimethylsilyl, THP or benzyl)),

12) -J^a-$COOR^{29}$ (in which R^{29} is as defined in claim 1 J^a is a single bond, -$(CH_2)_s$- or



(in which s is as defined in claim 1,
R^{30a} and R^{31a} each, independently, is i) hydrogen atom, ii) C1-8 alkyl, iii) -$COOR^{32}$ (in which R^{32} is as defined in claim 1), iv) carbocylic or heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, amino, nitro, hydroxy, protected hydroxy, halogen atom, nitrile, guanidino and amidino, or v) C1-8 alkyl substituted by one or more substituents selected from hydroxy, protected hydroxy, -$COOR^{33}$ (in which R^{33} is as defined in claim 1), -$NR^{34a}R^{35a}$ (in which R^{34a} and R^{35a} each, independently, is hydrogen atom (with the proviso that, R^{34a} and R^{35a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), carbocyclic or, heterocyclic ring, unsubstituted or substituted by one or more substituents selected from C1-4 alkyl, C1-4 alkoxyalkyl, protected amino, nitro, hydroxy, protected hydroxy, halogen atom, nitrile, guanidino and amidino, with the proviso that a carbon atom of C1-8 alkyl may be replaced by a sulfur atoms, or



in which R^{5a} and R^{6a}, taken together with the nitrogen atom to which they are attached represent a heterocyclic ring,
q is as defined in claim 1,
R^{15a} is
1) hydroxy,
2) hydroxy protected by a protecting group which is removable under acid conditions,
3) keto,
4) protected keto,
5) C1-4 alkyl,
6) C1-4 alkoxy,
7) phenyl,
8) phenoxy,
9) phenyl C1-4 alkyl,
10) phenyl C1-4 alkoxy,
11) nitro,
12) -$COOR^{36a}$ (in which R^{36a} is hydrogen atom, C1-8 alkyl, C1-4 alkyl substituted by -$CONR^{37}R^{38}$ (in which R^{37} and R^{38} are as defined in claim 1), C1-4 alkyl substituted by -$NR^{39a}R^{40a}$ (in which R^{39a} and R^{40a} each, independently, is hydrogen atom (with the proviso that, R^{39a} and R^{40a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), C1-4 alkyl substituted by -OR^{41a} (in which R^{41a} is C2-4 alkyl substituted by -OR^{42a} (in which R^{42a} is hydrogen atom, C2-4 alkoxyalkyl or benzyl) or C1-4 alkyl substituted by protected piperazino ring),
13) -$NR^{43a}R^{44a}$ (in which R^{43a} and R^{44a} each, independently, is hydrogen atom (with the proviso that, R^{43a} and R^{44a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl, C1-4 alkyl or C2-5 acyl),
14) -$CONR^{45a}R^{46a}$ (in which R^{45a} and R^{46a} each, independently, is hydrogen atom, C1-4 alkyl, hydroxy, hydroxy protected by a protecting group which is removable under acid conditions, phenyl C1-4 alkyloxy or C1-4 alkyl substituted by hydroxy, protected hydroxy or -$COOR^{47a}$ (in which R^{4a} is hydrogen atom, C1-8 alkyl or benzyl)),
15) C1-4 alkyl substituted by one or more substituents selected from hydroxy, protected hydroxy, -$COOR^{46a}$ (in which R^{46a} is hydrogen atom, C1-8 alkyl or benzyl), -$NR^{49a}R^{50a}$ (in which R^{49a} and R^{50a} each, independently, is hydrogen atom (with the proviso that, R^{49a} and R^{50a} do not represent hydrogen atom at the same time), t-butoxycarbonyl, benzyloxycarbonyl or C1-4 alkyl), or 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,

16) 5- or 6-membered heterocyclic ring containing one or two nitrogen atoms,
17) halogen atom,
18) -CHO protected by a protecting group which is removable under acid conditions, or
19) $-NR^{51a}-COOR^{52a}$ (in which R^{51a} and R^{52a} each, independently, is hydrogen atom or C1-8 alkyl), and the other symbols are as defined in claim 1, or
may be prepared by esterifying a compound of formula (II) with a compound of formula (III) to obtain a compound having protected group(s) and then eliminating the protecting groups,
or may be prepared by esterifying a compound of formula (II) with a compound of formula (III), if necessary, eliminating the protecting groups to obtain a compound having R^{15} represent C1-4 alkyl substituted by hydroxy, and then subjecting to sulfuric acid esterification and optionally converting a compound of formula (I) thus obtained into a non-toxic salt, acid addition salt or solvate thereof.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 96 30 7048

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Y,D	EP 0 484 949 A (CORTECH INC) 13 May 1992 * the whole document *	1-13	C07D403/12 A61K31/635 A61K31/40
Y,D	EP 0 465 802 A (CORTECH INC) 15 January 1992 * the whole document *	1-13	C07D207/06 C07C311/37 C07C311/44 C07D403/14
Y	WO 93 11760 A (CORTECH INC) 24 June 1993 * the whole document *	1-13	C07D413/12 C07D405/14 C07D417/12
Y	EP 0 539 223 A (ONO PHARMACEUTICAL CO) 28 April 1993 * the whole document *	1-13	C07D295/32 C07D207/28 C07D233/60 C07D401/12
Y,D	EP 0 347 168 A (ONO PHARMACEUTICAL CO) 20 December 1989 * the whole document *	1-13	C07D213/04 C07D207/32 C07D257/04 C07D211/10
Y	EP 0 222 608 A (ONO PHARMACEUTICAL CO) 20 May 1987 * the whole document *	1-13	
Y	TRENDS IN PHARMACOLOGICAL SCIENCE, vol. 8, August 1987, AMSTERDAM, pages 303-307, XP002024127 TRAINOR,D.A. : "Synthetic inhibitors of human neutrophil elastase " * the whole document *	1-13	TECHNICAL FIELDS SEARCHED (Int.Cl.6) C07D
Y	ANNU.REP.MED.CHEM., vol. 29, 1994, NEW YORK, pages 195-204, XP000650529 HLASTA,D.J. ET AL.: "Human Leukocyte Elastase Inhibitors" * the whole document *	1-13	

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	29 January 1997	Stellmach, J

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
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T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

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EUROPEAN SEARCH REPORT

Application Number
EP 96 30 7048

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
			C07D405/12 C07D207/16 C07D209/18 C07D409/12 C07D317/12 C07D333/24 C07D265/32 C07D213/64 C07D223/04 C07D233/06 //(C07D403/12, 207:00, 207:00), (C07D403/12, 209:00, 207:00), (C07D403/12, 233:00,
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
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Application Number
EP 96 30 7048

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
			207:00), (C07D403/12, 265:00, 207:00), (C07D403/12, 241:00, 207:00), (C07D403/12, 241:00, 207:00), (C07D403/12, 211:00,207:00)
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	29 January 1997	Stellmach, J

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